[1] *Sabnis RW*. **Novel Cyclic Tetramer Compounds as PCSK9 Inhibitors for Treating Metabolic Disorders**. ACS medicinal chemistry letters 2020; 11:1671-1673.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32944132
ABSTRACT

[2] *Arpaci A, Yalın S, Ecevit H et al.* **Enzyme activity and genetic polymorphisms in patients with type II diabetes mellitus**. Advances in clinical and experimental medicine : official organ Wroclaw Medical University 2020; 29:1057-1063.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32926601
ABSTRACT
BACKGROUND: Diabetes mellitus (DM) has become more and more common and has a high morbidity and mortality rate worldwide. It is a multifactorial chronic disease affected by both genetic and environmental factors. OBJECTIVES: To evaluate the association between antioxidant enzyme activities and their genetic variations and the level of malondialdehyde (MDA) in type II diabetes patients living in the Adıyaman province in the southeast part of Turkey. MATERIAL AND METHODS: One hundred patients diagnosed with type II DM (T2DM) and 100 healthy controls were included in the study. Malondialdehyde levels and antioxidant enzyme activities were measured spectrophometrically. DNA isolation was performed and genotyping was carried out using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). RESULTS: Our results revealed no significant differences in genotype distributions and allele frequencies of all polymorphisms between groups ($p > 0.05$). Significantly elevated MDA levels and a significant reduction in catalase (CAT) and paraoxonase (PON) enzyme activities were observed in patients compared to the control group in terms of study groups and genetic variations ($p < 0.05$). Moreover, CAT activity was reduced in TT genotype in terms of CAT -262 C/T polymorphism in patients ($p < 0.05$). Paraoxonase activity was observed to be lower in MM genotype in both groups ($p < 0.05$). CONCLUSIONS: CAT -262 C/T polymorphism may be one of the factors that lead to severe clinical situation in DM. Our results suggest that TT genotype may be more prone to lipid peroxidation.

[3] *Oh RC, Trivette ET, Westerfield KL*. **Management of Hypertriglyceridemia: Common Questions and Answers**. American family physician 2020; 102:347-354.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32931217
ABSTRACT
Hypertriglyceridemia, defined as fasting serum triglyceride levels of 150 mg per dL or higher, is associated with increased risk of cardiovascular disease. Severely elevated triglyceride levels (500 mg per dL or higher) increase the risk of pancreatitis. Common risk factors for hypertriglyceridemia include obesity, metabolic syndrome, and type 2 diabetes mellitus. Less common risk factors include excessive alcohol use, physical inactivity, being overweight, use of certain medications, and genetic disorders. Management of high triglyceride levels (150 to 499 mg per dL) starts with dietary changes and physical activity to lower cardiovascular risk. Lowering carbohydrate intake (especially refined carbohydrates) and increasing fat (especially omega-3 fatty acids) and protein intake can lower triglyceride levels. Moderate- to high-intensity physical activity can lower triglyceride levels, as well as improve body composition and exercise capacity. Calculating a patient's 10-year risk of atherosclerotic cardiovascular disease is pertinent to determine the role of medications. Statins can be considered for

patients with high triglyceride levels who have borderline (5% to 7.4%) or intermediate (7.5% to 19.9%) risk. For patients at high risk who continue to have high triglyceride levels despite statin use, high-dose icosapent (purified eicosapentaenoic acid) can reduce cardiovascular mortality (number needed to treat = 111 to prevent one cardiovascular death over five years). Fibrates, omega-3 fatty acids, or niacin should be considered for patients with severely elevated triglyceride levels to reduce the risk of pancreatitis, although this has not been studied in clinical trials. For patients with acute pancreatitis associated with hypertriglyceridemia, insulin infusion and plasmapheresis should be considered if triglyceride levels remain at 1,000 mg per dL or higher despite conservative management of acute pancreatitis.

[4] *Taylan C, Driemeyer J, Schmitt CP et al.* **Cardiovascular Outcome of Pediatric Patients With Bi-Allelic (Homozygous) Familial Hypercholesterolemia Before and After Initiation of Multimodal Lipid Lowering Therapy Including Lipoprotein Apheresis**. The American journal of cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32946862
ABSTRACT
Twenty-four patients with bi-allelic familial hypercholesterolemia commencing chronic lipoprotein apheresis (LA) at a mean age of 8.5 ± 3.1 years were analysed retrospectively and in part prospectively with a mean follow-up of 17.2 ± 5.6 years. Mean age at diagnosis was 6.3 ± 3.4 years. Untreated mean LDL-C concentrations were 752 mg/dl ± 193 mg/dl (19.5 mmol/l ± 5.0 mmol/l). Multimodal lipid lowering therapy including LA resulted in a mean LDL-C concentration of 184 mg/dl (4.8 mmol/l), which represents a 75.5% mean reduction. Proprotein convertase subtilisin/kexin type 9-antibodies contributed in 3 patients to LDL-C lowering with 5 patients remaining to be tested. After commencing chronic LA, 16 patients (67%) remained clinically stable with only subclinical findings of atherosclerotic cardiovascular disease (ASCVD), and neither cardiovascular events, nor need for vascular interventions or surgery. In 19 patients (79%), pathologic findings were detected at the aortic valve (AV), which in the majority were mild. AV replacement was required in 2 patients. Mean Lipoprotein(a) concentration was 42.4 mg/dl, 38% had >50 mg/dl. There was no overt correlation of AV pathologies with other ASCVD complications, or Lipoprotein(a) concentration. Physicochemical elimination of LDL particles by LA appears indispensable for patients with bi-allelic familial hypercholesterolemia and severe hypercholesterolemia to maximize the reduction of LDL-C. In conclusion, in this rare patient group regular assessment of both the AV, as well as all arteries accessible by ultrasound should be performed to adjust the intensity of multimodal lipid lowering therapy with the goal to prevent ASCVD events and aortic surgery.

[5] *Eraikhuemen N, Lazaridis D, Dutton MT*. **Emerging Pharmacotherapy to Reduce Elevated Lipoprotein(a) Plasma Levels**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32929693
ABSTRACT
Lipoprotein(a) is a unique form of low-density lipoprotein. It is associated with a high incidence of premature atherosclerotic disease such as coronary artery disease, myocardial infarction, and stroke. Plasma levels of this lipoprotein and its activities are highly variable. This is because of a wide variability in the size of the apolipoprotein A moiety, which is determined by the number of repeats of cysteine-rich domains known as "kringles." Although the exact

mechanism of lipoprotein(a)-induced atherogenicity is unknown, the lipoprotein has been found in the arterial walls of atherosclerotic plaques. It has been implicated in the formation of foam cells and lipid deposition in these plaques. Pharmacologic management of elevated levels of lipoprotein(a) with statins, fibrates, or bile acid sequestrants is ineffective. The newer and emerging lipid-lowering agents, such as the second-generation antisense oligonucleotides, cholesteryl ester transfer protein inhibitors, and proprotein convertase subtilisin/kexin type 9 inhibitors offer the most effective pharmacologic therapy.

[6] *Matta A, Taraszkiewicz D, Bongard V, Ferrières J*. **Ineffective Subtilisin/Kexin Type 9 (PCSK9) Inhibitors Monotherapy in Dyslipidemia with Low-Density Lipoprotein Cholesterol (LDL-C) Receptor Abnormalities: A Report of 2 Cases**. Am J Case Rep 2020; 21:e923722.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32929056
ABSTRACT
BACKGROUND Real-life data on the efficacy of monotherapy with PCSK9 inhibitors are scarce. Most cohort studies have examined populations that are not severely dyslipidemic and are receiving combined therapy rather than monotherapy. CASE REPORT From a series of 167 alirocumab prescriptions, we present a case of complete nonresponse and one of low response to monotherapy with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors in 2 patients with heterozygous familial hypercholesterolemia and abnormalities of the low-density lipoprotein cholesterol (LDL-C) receptor. In these cases, PCSK9 inhibitors were ineffective when used alone to reduce the LDL-C level, but the addition of statin led to a dramatic improvement. CONCLUSIONS As PCSK9 inhibitors become more commonly prescribed, more cases of nonresponse to PCSK9 inhibitors will be identified. Prospective studies are needed to investigate the efficacy of treatment with the monoclonal antibodies PCSK9 inhibitors in the context of LDL-C receptor abnormalities and to determine whether a genetic explanation exists for interindividual differences in response.

[7] *Tong S, Kaitu'u-Lino TJ, Hastie R et al.* **Pravastatin, proton-pump inhibitors, metformin, micronutrients, and biologics: new horizons for the prevention or treatment of preeclampsia**. American journal of obstetrics and gynecology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32946849
ABSTRACT
There has been increasing research momentum to identify new therapeutic agents for the prevention or treatment of preeclampsia, drugs that can affect the underlying disease pathophysiology. Molecular targets of candidate treatments include oxidative stress, antiangiogenic factors, and the angiotensin, nitric oxide, and proinflammatory pathways. The proposed treatments undergoing preclinical and clinical trial evaluation are thought to act on placental or endothelial disease or both. Most have adopted the pragmatic strategy of repurposing drugs. Of all the therapeutic agents proposed, pravastatin has received the most interest. There are preclinical studies showing that it has pleiotropic actions that favorably impact on multiple molecular targets and can resolve a preeclampsia phenotype in many animal models. An early phase clinical trial suggests that it may have therapeutic activity. Several large prevention trials are planned or ongoing and, when completed, could definitively address whether pravastatin can prevent preeclampsia. Proton-pump inhibitors, metformin, and sulfasalazine are other drugs with preclinical evidence of multiple molecular actions that

could resolve the pathophysiology of preeclampsia. These agents are also currently being evaluated in clinical trials. There have been many recent preclinical studies identifying the potential of numerous natural compounds to treat preeclampsia, such as plant extracts and micronutrients that have potent anti-inflammatory or antioxidant activity. Recent preclinical studies have also proposed novel molecular-targeted strategies, such as monoclonal antibodies targeting tumor necrosis factor alpha, placental growth factor, and short interfering RNA technology, to silence the gene expression of soluble fms-like tyrosine kinase-1 or angiotensinogen. Other treatment approaches that have transitioned to human trials (ranging from single-arm to phase III trials that have been completed or are ongoing) include folic acid, nitric oxide donors (such as L-arginine), recombinant antithrombin III, digoxin immune antigen-binding fragment, and melatonin. There have been case series showing the removal of circulating soluble fms-like tyrosine kinase-1 may help stabilize the disease and prolong pregnancy. Interestingly, there are case reports suggesting that monoclonal antibody eculizumab (complement inhibitor) may have therapeutic potential. If new agents are discovered that are proven to be effective in preventing or treating preeclampsia, the potential to improve global maternal and perinatal health will be significant.

[8] *Huang Y, Ning K, Li WW et al.* **Hydrogen Sulfide Accumulates LDL Receptor Precursor via Downregulating PCSK9 in HepG2 Cells**. Am J Physiol Cell Physiol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32938225

ABSTRACT

Endogenous hydrogen sulfide (H(2)S) affects cholesterol homeostasis and liver X receptor α (LXRα) expression. However, whether low density lipoprotein (LDL) receptor (LDLR), a key player in cholesterol homeostasis, is regulated by exogenous H(2)S through LXRα signaling has not been determined. We investigated the effects of sodium hydrosulfide (NaHS, H(2)S donor) on LDLR expression in the presence or absence of LXR agonists, T0901317 or GW3965 in HepG2 cells. We found that H(2)S strongly accumulated LDLR precursor in the presence of T0901317. Hence LDLR transcription and the genes involved in LDLR precursor maturation and degradation were studied. T0901317 increased the LDLR mRNA level, while H(2)S didn't affect LDLR transcription. H(2)S had no significant effect on the expression of LXRα and inducible degrader of LDLR (IDOL). H(2)S and T0901317 altered mRNA levels of several enzymes for N- and O-glycosylation and endoplasmic reticulum (ER) chaperones assisting LDLR maturation, but didn't affect their protein levels. H(2)S decreased proprotein convertase subtilisin/kexin type 9 (PCSK9) protein levels and its mRNA level elevated by T0901317. T0901317 with PCSK9 siRNA also accumulated LDLR precursor as did T0901317 with H(2)S. High glucose increased PCSK9 protein levels and attenuated LDLR precursor accumulation induced by T0901317 with H(2)S. Taken together, H(2)S accumulates LDLR precursor by downregulating PCSK9 expression but not through the LXRα-IDOL pathway, LDLR transcriptional activation or dysfunction of glycosylation enzymes and ER chaperones. These results also indicate that PCSK9 plays an important role in LDLR maturation in addition to its well-known effect on the degradation of LDLR mature form.

[9] *Toth PP, Shah PK, Lepor NE*. **Targeting hypertriglyceridemia to mitigate cardiovascular risk: A review**. Am J Prev Cardiol 2020; 3:100086.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32929418

ABSTRACT

A causal relationship between elevated triglycerides and cardiovascular disease is controversial, as trials of triglyceride-lowering treatments have not shown significant impact on cardiovascular outcomes. However, hypertriglyceridemia is associated with atherogenesis and risk for acute cardiovascular events that persist despite optimal statin treatment. Although most trials of triglyceride-lowering treatments have been negative, in trials of niacin and fibrates, subgroup analyses in patients with higher baseline triglycerides and lower HDL-C levels suggest reduced incidence of cardiovascular endpoints. The REDUCE-IT trial demonstrated that addition of purified prescription eicosapentaenoic acid (icosapent ethyl) 4 g/day in high-risk patients with triglyceride levels 135-499 mg/dL and optimized statin treatment significantly reduced cardiovascular events versus placebo (hazard ratio 0.75; 95% confidence interval 0.68-0.83; P < 0.001). Benefit was seen regardless of baseline and on-treatment triglyceride levels, suggesting that other effects of eicosapentaenoic acid besides triglyceride reduction may have played a role.

[10] *Thadchanamoorthy V, Dayasiri K, Majitha SI et al.* **Homozygous autosomal recessive hypercholesterolaemia in a South Asian child presenting with multiple cutaneous xanthomata**. Annals of clinical biochemistry 2020:4563220961755.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32936664
ABSTRACT
Autosomal recessive hypercholesterolemia (ARH; OMIM #603813) is an extremely rare disorder of lipid metabolism caused by loss-of-function variants in the LDL receptor adapter protein 1 (LDLRAP1) gene, which is characterized by severe hypercholesterolaemia and an increased risk of premature atherosclerotic cardiovascular disease. We report the case of an 11-year-old girl who presented with multiple painless yellowish papules around her elbows and knees of two-year duration. She had been reviewed by several general practitioners, with some of the papules having been excised, but without a specific diagnosis being made. The child was referred to a paediatric service for further evaluation and treatment of the cutaneous lesions, which appeared xanthomatous in nature. A lipid profile showed severe hypercholesterolaemia. Next generation sequencing analysis of a monogenic hypercholesterolaemia gene panel revealed homozygosity for a pathogenic frameshift mutation, c.71dupG, p.Gly25Argfs*9 in LDLRAP1. Her parents and brother, who were asymptomatic, were screened and found to be heterozygous carriers of the LDLRAP1 variant. There was no known consanguinity in the family. She was commenced on the HMG-CoA reductase inhibitor, atorvastatin, to good effect, with a ~76% reduction in LDL-cholesterol at a dose of 50 mg per day. At six-month follow-up, there had been no obvious regression of the xanthomata, but importantly, no enlargement of, or the development of new papular lesions, have occurred. In summary, we report a child who presented with multiple cutaneous xanthomata and was confirmed to have ARH by the presence of a homozygous novel pathogenic frameshift variant in LDLRAP1.

[11] *Ignatyev IM, Gafurov MR, Krivosheeva NV*. **Criteria for Carotid Atherosclerotic Plaque Instability**. Annals of vascular surgery 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32927044
ABSTRACT
BACKGROUND: The study aim is to determine the criteria for carotid atherosclerotic plaque instability with the use of an advanced ultrasound technology, immunohistochemical analysis,

and electron paramagnetic resonance (EPR) and assess their correlations with histologic results. METHODS: A total of 92 patients were included in the study and were examined by ultrasound duplex scanning and ultrasound elastography. Plaques harvested during carotid endarterectomy were obtained for histologic analysis, immunofluorescent assay, and EPR spectroscopic measurements. RESULTS: Multivariate logistic regression analysis showed that plaques with an area >90 mm(2) (odds ratio [OR], 4.05; 95% confidence interval [CI], 1.32-13.2; P = 0.006), plaque volume index > 0.6 cm(3) (OR, 2.72; 95% CI, 1.05-9.58; P = 0.04), and juxtaluminal black area ≥8 mm(2) (OR, 2.82; 95% CI, 1.22-6. 23; P = 0.02) were statistically significant independent predictors of histologically verified unstable plaques. Unstable plaques occurred in 94% of the patients with these indicators. Significant increases in the number of CD68+ and CD36+ cells (inflammatory markers) and CD31+ cells (neovasculogenesis markers) were revealed in unstable plaques by the immunohistochemical assay. EPR data analysis showed that divalent manganese could serve as a marker of plaque instability. CONCLUSIONS: Additional ultrasound criteria, verified by histologic studies, significantly increased the information content for identifying patients with unstable plaques, which can be of great importance in stratifying the risk of ischemic stroke, especially in asymptomatic patients. The degree of calcification is not a mandatory criterion for plaque stabilization.

[12] *Shrungeswara AH, Unnikrishnan MK*. **Energy provisioning and inflammasome activation: The pivotal role of AMPK in sterile inflammation and associated metabolic disorders**. Anti-inflammatory & anti-allergy agents in medicinal chemistry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32938355
ABSTRACT
BACKGROUND: Body defenses and metabolic processes probably co-evolved in such a way that rapid, energyintensive acute inflammatory repair is functionally integrated with energy allocation in a starvation/ infection / injury-prone primitive environment. Disruptive metabolic surplus, aggravated by sedentary lifestyle, induces chronic under-activation of AMPK, the master regulator of intracellular energy homeostasis. Sudden increase in chronic, dysregulated 'sterile' inflammatory disorders probably results from a shift towards calorie rich, sanitized, cushioned, injury/ infection free environment, repositioning inflammatory repair pathways towards chronic, non-microbial, 'sterile', 'low grade', 'parainflammation'. AMPK, (at the helm of energy provisioning) supervises the metabolic regulation of inflammasome activation, a common denominator in lifestyle disorders. DISCUSSION: In this review we discuss various pathways linking AMPK under-activation and inflammasome activation. AMPK under-activation, the possible norm in energy-rich sedentary lifestyle, could be the central agency that stimulates inflammasome activation by multiple pathways such as: [1] decreasing autophagy, and accumulation of intracellular DAMPs, (particulate crystalline molecules, advanced glycation end-products, oxidized lipids etc.) [2] stimulating a glycolytic shift (pro-inflammatory) in metabolism, [3] promoting NF-kB activation and decreasing Nrf2 activation, [4] increasing reactive oxygen species (ROS) formation, unfolded protein response(UPR) and endoplasmic reticulum (ER) stress. CONCLUSION: The 'inverse energy crisis', associated with calorie-rich, sedentary lifestyle, advocates dietary and pharmacological interventions for treating chronic metabolic disorders by overcoming / reversing AMPK under-activation.

[13] *Harrison SL, Lane DA, Banach M et al.* **Lipid levels, atrial fibrillation and the impact of age: Results from the LIPIDOGRAM2015 study**. Atherosclerosis 2020; 312:16-22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32947222
ABSTRACT
BACKGROUND AND AIMS: An inverse relationship between lipid levels and atrial fibrillation (AF) has been suggested, but whether the association is upheld for all age groups remains unclear. The aim of the study was to examine associations between lipid levels and AF by age groups in a nationwide study in Poland. METHODS: Multivariate Poisson regression models were used to estimate prevalence ratios (PRs) for AF by lipid levels. Low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), total cholesterol (TC), non-HDL-C and LDL-C/HDL-C ratios were grouped into quartiles. RESULTS: Of the 13,724 participants, 5.2% (n = 708) had AF. People with AF were older with more comorbidities, but lower lipid levels (all $p < 0.05$). The prevalence of AF was inversely associated with LDL-C (Adjusted PR (95% Confidence Interval) highest versus lowest quartile: 0.60 (0.48, 0.75)), TC (0.61 (0.49, 0.75)) and non-HDL-C (0.63 (0.51, 0.78)). The prevalence of AF was inversely associated with HDL-C (0.58 (0.46, 0.74)), but this was not statistically significant for people aged 75 years and older. For the LDL-C/HDL-C ratio, the prevalence of AF was only inversely associated with higher levels for people aged 75 years and older (0.75 (0.61, 0.94)). There was no statistically significant difference in prevalence of AF by TG levels. CONCLUSIONS: The results suggest an inverse relationship between lipid levels and AF. The inverse association between higher HDL-C and AF was only significant for people aged <75 years, whereas the inverse association between higher LDL-C/HDL-C ratio and AF was only significant for people aged 75 years and older.

[14] *Majeed K, Hillis GS, Schultz CJ*. **A "light based biopsy" for high-risk atherosclerotic plaque**. Atherosclerosis 2020; 309:65-66.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32921431
ABSTRACT

[15] *Pepplinkhuizen S, Ibrahim S, Vink R et al.* **Electronic health records to facilitate continuous detection of familial hypercholesterolemia**. Atherosclerosis 2020; 310:83-87.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32927124
ABSTRACT
BACKGROUND AND AIMS: Familial hypercholesterolemia (FH) is an inherited disorder associated with increased risk of coronary heart disease as a result of high LDL-cholesterol (LDL-C). The clinical diagnosis can be made with the Dutch Lipid Clinic Network criteria (DLCN criteria). FH is an underdiagnosed disorder, possibly due to false negative LDL-C interpretation during lipid lowering therapy (LLT). We hypothesized that automated health record-based integration of data can provide a signal to facilitate identification of FH patients. METHODS: We included patients with LDL-C ≥6.5 mmol/l after correction for LLT in all patients testing LDL-C in Northwest Clinics, The Netherlands. Patients previously diagnosed with FH were excluded. The primary endpoint was the additional number of patients with DLCN criteria ≥6 points after correction for LLT. Secondary endpoints were the additional number of patients with DLCN criteria ≥6 points after also adding data on patient- and family history, and LDL-C before and after correction for LLT. Analysis was performed in a daily automated routine (HiX ChipSoft). RESULTS: In a total of 41,937 individual LDL-C measurements during 26 weeks,

we found 351 patients with LDL-C ≥6.5 mmol/l after automated correction for LLT. FH had previously been diagnosed in 42 patients. In the remaining 309 patients (58.3% female; age: 66 ± 11 yrs (mean ± SD); 85.8% on LLT), the number of patients with DLCN criteria ≥6 points increased from 9 to 95 after correction for LLT, and to 127 after also adding patient and family history. The mean LDL-C before and after correction for LLT was 4.69 ± 1.42 mmol/l and 8.16 ± 1.68 mmol/l, respectively (mean ± SD; $p < 0.001$). CONCLUSIONS: We conclude that automated medical record-based integration of LDL-C, LLT and patient- and family history can provide a crucial signal to facilitate identification of FH. Whether this signal results in subsequent genetic identification of FH patients and their relatives requires further study.

[16] *Lefkou E, Varoudi K, Pombo J et al.* **Triple therapy with pravastatin, low molecular weight heparin and low dose aspirin improves placental haemodynamics and pregnancy outcomes in obstetric antiphospholipid syndrome in mice and women through a nitric oxide-dependent mechanism**. Biochem Pharmacol 2020; 182:114217.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32926874

ABSTRACT

OBJECTIVES: A previous pilot study showed that pravastatin supplementation improved pregnancy outcomes in women with obstetric antiphospholipid syndrome (OAPS) that developed placental insufficiency despite standard of care treatment low molecular weight heparin plus low dose aspirin (LMWH + LDA). In this study we investigated the mechanism behind the beneficial effects of the triple therapy LMWH + LDA + pravastatin in improving uteroplacental vascular function and reducing pregnancy complications in OAPS. We hypothesized that nitric oxide (NO) is involved in the vasculoprotective effects of the triple therapy. A mouse model of OAPS that resembles the clinical scenario was used to test this hypothesis. METHODS: Eleven women with OAPS that developed preeclampsia (PE) and/or intrauterine growth restriction (IUGR) associated with uteroplacental vascular dysfunction despite treatment with LMWH + LDA participated in this study after given informed written consent. Seven women were supplemented with pravastatin at the time abnormal uterine artery Dopplers were detected and 4 remained on LMWH + LDA treatment only. Wire myography was used to identify the mechanisms underpinning the protective effects of the triple therapy in the mouse model of OAPS. RESULTS: The triple therapy increased serum NO levels, diminished uteroplacental vessels resistance improving placental function and prolonged pregnancies compared to conventional treatment LMWH + LDA, leading to live births in women with OAPS. Comparable to the observations in women, the triple therapy protected pregnancies in OAPS-mice, increasing placental perfusion and pregnancy outcomes. A synergistic vasculoprotective effect of the triple therapy on uterine arteries and aorta was demonstrated in OAPS-mice. LMWH + LDA showed a partial protection on endothelial function. Addition of pravastatin increase eNOS synthesis, expression and activity/signaling leading to a significant increment in nitric oxide (NO) generation, resulting in improved placental vascular function and total protection of pregnancies. CONCLUSION: LMWH + LDA + PRAV increased serum NO levels and significantly improved placental haemodynamics and maternal and neonatal outcomes in women and mice with OAPS. A role for eNOS/NO in mediating the placental vasculoprotective effects in OAPS-mice was demonstrated, strengthening the concept that impaired NO production is a crucial mediator in the pathogenesis of OAPS and a potential target for pharmacological interventions. The efficacy of pravastatin supplementation should be confirmed in a larger clinical trial.

[17] *Alannan M, Fayyad-Kazan H, Trézéguet V, Merched A*. **Targeting Lipid Metabolism in Liver Cancer**. Biochemistry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32930581
ABSTRACT
Cancer cells are highly dependent on different metabolic pathways for sustaining their survival, growth, and proliferation. Lipid metabolism not only provides the energetic needs of the cells but also provides the raw material for cellular growth and the signaling molecules for many oncogenic pathways. Mainly processed in the liver, lipids play an essential role in the physiology of this organ and in the pathological progression of many diseases such as metabolic syndrome and hepatocellular carcinoma (HCC). The progression of HCC is associated with inflammation and complex metabolic reprogramming, and its prognosis remains poor because of the lack of effective therapies despite many years of dedicated research. Defects in hepatic lipid metabolism induce abnormal gene expression and rewire many cellular pathways involved in oncogenesis and metastasis, implying that interfering with lipid metabolism within the tumor and the surrounding microenvironment may be a novel therapeutic approach for treating liver cancer patients. Therefore, this review focuses on the latest advances in drugs targeting lipid metabolism and leading to promising outcomes in preclinical studies and some ongoing clinical trials.

[18] *Ahmadi M, Amiri S, Pecic S et al.* **Pleiotropic effects of statins: A focus on cancer**. Biochimica et biophysica acta. Molecular basis of disease 2020; 1866:165968.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32927022
ABSTRACT
The statin drugs ('statins') potently inhibit hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase by competitively blocking the active site of the enzyme. Statins decrease de novo cholesterol biosynthesis and thereby reduce plasma cholesterol levels. Statins exhibit "pleiotropic" properties that are independent of their lipid-lowering effects. For example, preclinical evidence suggests that statins inhibit tumor growth and induce apoptosis in specific cancer cell types. Furthermore, statins show chemo-sensitizing effects by impairing Ras family GTPase signaling. However, whether statins have clinically meaningful anti-cancer effects remains an area of active investigation. Both preclinical and clinical studies on the potential mechanisms of action of statins in several cancers have been reviewed in the literature. Considering the contradictory data on their efficacy, we present an up-to-date summary of the pleiotropic effects of statins in cancer therapy and review their impact on different malignancies. We also discuss the synergistic anti-cancer effects of statins when combined with other more conventional anti-cancer drugs to highlight areas of potential therapeutic development.

[19] *Garcia-Sabaté A, Mohamed WKE, Sapudom J et al.* **Biomimetic 3D Models for Investigating the Role of Monocytes and Macrophages in Atherosclerosis**. Bioengineering (Basel) 2020; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32947976
ABSTRACT
Atherosclerosis, the inflammation of artery walls due to the accumulation of lipids, is the most common underlying cause for cardiovascular diseases. Monocytes and macrophages are

major cells that contribute to the initiation and progression of atherosclerotic plaques. During this process, an accumulation of LDL-laden macrophages (foam cells) and an alteration in the extracellular matrix (ECM) organization leads to a local vessel stiffening. Current in vitro models are carried out onto two-dimensional tissue culture plastic and cannot replicate the relevant microenvironments. To bridge the gap between in vitro and in vivo conditions, we utilized three-dimensional (3D) collagen matrices that allowed us to mimic the ECM stiffening during atherosclerosis by increasing collagen density. First, human monocytic THP-1 cells were embedded into 3D collagen matrices reconstituted at low and high density. Cells were subsequently differentiated into uncommitted macrophages (M0) and further activated into pro- (M1) and anti-inflammatory (M2) phenotypes. In order to mimic atherosclerotic conditions, cells were cultured in the presence of oxidized LDL (oxLDL) and analyzed in terms of oxLDL uptake capability and relevant receptors along with their cytokine secretomes. Although oxLDL uptake and larger lipid size could be observed in macrophages in a matrix dependent manner, monocytes showed higher numbers of oxLDL uptake cells. By analyzing major oxLDL uptake receptors, both monocytes and macrophages expressed lectin-like oxidized low-density lipoprotein receptor-1 (LOX1), while enhanced expression of scavenger receptor CD36 could be observed only in M2. Notably, by analyzing the secretome of macrophages exposed to oxLDL, we demonstrated that the cells could, in fact, secrete adipokines and growth factors in distinct patterns. Besides, oxLDL appeared to up-regulate MHCII expression in all cells, while an up-regulation of CD68, a pan-macrophage marker, was found only in monocytes, suggesting a possible differentiation of monocytes into a pro-inflammatory macrophage. Overall, our work demonstrated that collagen density in the plaque could be one of the major factors driving atherosclerotic progression via modulation of monocyte and macrophages behaviors.

[20] *Dickens AM, Sen P, Kempton MJ et al.* **Dysregulated Lipid Metabolism Precedes Onset of Psychosis**. Biol Psychiatry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32928501
ABSTRACT
BACKGROUND: A key clinical challenge in the management of individuals at clinical high risk for psychosis (CHR) is that it is difficult to predict their future clinical outcomes. Here, we investigated if the levels of circulating molecular lipids are related to adverse clinical outcomes in this group. METHODS: Serum lipidomic analysis was performed in 263 CHR individuals and 51 healthy control subjects, who were then clinically monitored for up to 5 years. Machine learning was used to identify lipid profiles that discriminated between CHR and control subjects, and between subgroups of CHR subjects with distinct clinical outcomes. RESULTS: At baseline, compared with control subjects, CHR subjects (independent of outcome) had higher levels of triacylglycerols with a low acyl carbon number and a double bond count, as well as higher levels of lipids in general. CHR subjects who subsequently developed psychosis (n = 50) were distinguished from those that did not (n = 213) on the basis of lipid profile at baseline using a model with an area under the receiver operating curve of 0.81 (95% confidence interval = 0.69-0.93). CHR subjects who became psychotic had lower levels of ether phospholipids than CHR individuals who did not ($p < .01$). CONCLUSIONS: Collectively, these data suggest that lipidomic abnormalities predate the onset of psychosis and that blood lipidomic measures may be useful in predicting which CHR individuals are most likely to develop psychosis.

[21] *Martín-Campos JM, Ruiz-Nogales S, Ibarretxe D et al.* **Polygenic Markers in Patients Diagnosed of Autosomal Dominant Hypercholesterolemia in Catalonia: Distribution of Weighted LDL-c-Raising SNP Scores and Refinement of Variant Selection**. Biomedicines 2020; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32942679
ABSTRACT
Familial hypercholesterolemia (FH) is associated with mutations in the low-density lipoprotein (LDL) receptor (LDLR), apolipoprotein B (APOB), and proprotein convertase subtilisin/kexin 9 (PCSK9) genes. A pathological variant has not been identified in 30-70% of clinically diagnosed FH patients, and a burden of LDL cholesterol (LDL-c)-raising alleles has been hypothesized as a potential cause of hypercholesterolemia in these patients. Our aim was to study the distribution of weighted LDL-c-raising single-nucleotide polymorphism (SNP) scores (weighted gene scores or wGS) in a population recruited in a clinical setting in Catalonia. The study included 670 consecutive patients with a clinical diagnosis of FH and a prior genetic study involving 250 mutation-positive (FH/M+) and 420 mutation-negative (FH/M-) patients. Three wGSs based on LDL-c-raising variants were calculated to evaluate their distribution among FH patients and compared with 503 European samples from the 1000 Genomes Project. The FH/M- patients had significantly higher wGSs than the FH/M+ and control populations, with sensitivities ranging from 42% to 47%. A wGS based only on the SNPs significantly associated with FH (wGS8) showed a higher area under the receiver operating characteristic curve, and higher diagnostic specificity and sensitivity, with 46.4% of the subjects in the top quartile. wGS8 would allow for the assignment of a genetic cause to 66.4% of the patients if those with polygenic FH are added to the 37.3% of patients with monogenic FH. Our data indicate that a score based on 8 SNPs and the75th percentile cutoff point may identify patients with polygenic FH in Catalonia, although with limited diagnostic sensitivity and specificity.

[22] *Bonaterra GA, Bender K, Wilhelm B et al.* **Effect of cholesterol re-supplementation and atorvastatin on plaque composition in the thoracic aorta of New Zealand white rabbits**. BMC cardiovascular disorders 2020; 20:420.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32942987
ABSTRACT
BACKGROUND: Effects of re-supplementation of a cholesterol-enriched diet (CEDrs) on size, cholesterol content and morphology of already existing plaques are not known to date. METHODS: A group of rabbits received standard chow (SC) for 6 weeks ("negative control"; for plasma lipid measurements only). Group I-IV received 2% CED (induction) for 6 weeks; thereafter, groups II-IV have been fed a SC (= cholesterol withdrawal) for 68 weeks. Afterwards, feeding of groups II-IV was continued as follows: Group II - 10 weeks SC, group III - 4 weeks 0.5% CED (~re-supplementation), afterwards 6 weeks SC (~withdrawal again); group IV - 4 weeks 0.5% CED (re-supplementation) + atorvastatin (2.5 mg/kg body weight/day), afterwards 6 weeks SC (~withdrawal again) + atorvastatin. Plasma lipids, but also plaque size, morphology and cholesterol contents of thoracic aortas were quantified. RESULTS: After CEDrs, plasma cholesterol levels were increased. However, after withdrawal of CEDrs, plasma cholesterol levels decreased, whereas the cholesterol content of the thoracic aorta was increased in comparison with the group without CEDrs. Plaque size remained unaffected.

Atorvastatin application did not change plasma cholesterol level, cholesterol content of the thoracic aorta and plaque size in comparison with the group without drug treatment. However, atorvastatin treatment increased the density of macrophages (MΦ) compared with the group without treatment, with a significant correlation between densities of MΦ (Mac-1(+)) and apoptotic (TUNEL(+); TP53(+)), antigen-presenting (HLA-DR(+)) or oxidatively stressed (SOD2(+)) cells. CONCLUSIONS: In rabbits with already existing plaques, CEDrs affects plaque morphology and cellular composition, but not plaque size. Despite missing effects on plasma cholesterol levels, cholesterol content of the thoracic aorta and size of already existing atherosclerotic plaques, atorvastatin treatment transforms the already existing lesions to a more active form, which may accelerate the remodelling to a more stable plaque.

[23] *Habib A, Habib A*. **No association between subclinical hypothyroidism and dyslipidemia in children and adolescents**. BMC pediatrics 2020; 20:436.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32938413
ABSTRACT
BACKGROUND: There are controversies about the correlation between higher levels of thyroid stimulating hormone (TSH) and dyslipidemia in children. This study was designed to assess the relation between lipid profile components and TSH levels in children. METHOD: This cross-sectional study was performed in a pediatric endocrinology growth assessment clinic in Shiraz, southern Iran. Children aged 2-18 years who referred to the clinic from January until April 2018 were included. TSH levels equal or above 5 mIU/L and lower than 10 mIU/L with normal free T4 (FT4) were considered as having subclinical hypothyroidism (SH). RESULTS: Six hundred sixty-six children were euthyroid while 181 had SH. No significant difference was found between the mean serum total cholesterol (P = 0.713), LDL-C (P = 0.369), HDL-C (P = 0.211), non-HDL-C (P = 0.929), and triglyceride (P = 0.215) levels between euthyroid children and subjects with SH. There was also no significant difference in the prevalence of dyslipidemias in any lipid profile components between the two groups. The adjusted correlation was not significant between TSH levels and any lipid profile component. CONCLUSION: Based on the results of our study, we found no correlation between SH and dyslipidemia in children. The association between dyslipidemia and SH in children still seems to be inconsistent based on the results of this and previous studies. We recommend a meta-analysis or a significantly larger retrospective study on this subject.

[24] *Xu HB, Wang J, Chen JL et al.* **Impacts of smoking status on the clinical outcomes of coronary non-target lesions in patients with coronary heart disease: a single-center angiographic study**. Chinese medical journal 2020; 133:2295-2301.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32925280
ABSTRACT
BACKGROUND: Coronary atherosclerotic plaque could go through rapid progression and induce adverse cardiac events. This study aimed to evaluate the impacts of smoking status on clinical outcomes of coronary non-target lesions. METHODS: Consecutive patients with coronary heart disease who underwent two serial coronary angiographies were included. All coronary non-target lesions were recorded at first coronary angiography and analyzed using quantitative coronary angiography at both procedures. Patients were grouped into non-smokers, quitters, and smokers according to their smoking status. Clinical outcomes including rapid lesion progression, lesion re-vascularization, and myocardial infarction were recorded at

second coronary angiography. Multivariable Cox regression analysis was used to investigate the association between smoking status and clinical outcomes. RESULTS: A total of 1255 patients and 1670 lesions were included. Smokers were younger and more likely to be male compared with non-smokers. Increase in percent diameter stenosis was significantly lower (2.7 [0.6, 7.1] % vs. 3.5 [0.9, 8.9]%) and 3.4 [1.1, 7.7]%, P=0.020) in quitters than those in smokers and non-smokers. Quitters tended to have a decreased incidence of rapid lesions progression (15.8% [76/482] vs. 21.6% [74/342] and 20.6% [89/431], P=0.062), lesion re-vascularization (13.1% [63/482] vs. 15.5% [53/432] and 15.5% [67/431], P=0.448), lesion-related myocardial infarction (0.8% [4/482] vs. 2.6% [9/342] and 1.4% [6/431], P=0.110) and all-cause myocardial infarction (1.9% [9/482] vs. 4.1% [14/342] and 2.3% [10/431], P=0.128) compared with smokers and non-smokers. In multivariable analysis, smoking status was not an independent predictor for rapid lesion progression, lesion re-vascularization, and lesion-related myocardial infarction except that a higher risk of all-cause myocardial infarction was observed in smokers than non-smokers (hazards ratio: 3.00, 95% confidence interval: 1.04-8.62, P=0.042). CONCLUSION: Smoking cessation mitigates the increase in percent diameter stenosis of coronary non-target lesions, meanwhile, smokers are associated with increased risk for all-cause myocardial infarction compared with non-smokers.

[25] *Su X, Li G, Deng Y, Chang D*. **Cholesteryl ester transfer protein inhibitors in precision medicine**. Clinica chimica acta; international journal of clinical chemistry 2020; 510:733-740. **PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=32941836

ABSTRACT

Dyslipidemia is associated with atherosclerosis and cardiovascular disease development, posing serious risks to human health. Cholesteryl ester transfer protein (CETP) is responsible for exchange of neutral lipids, such as cholesteryl ester and TG, between plasma high density lipoprotein (HDL) particles and Apolipoprotein B-100 (ApoB-100) containing lipoprotein particles. Genetic studies suggest that single-nucleotide polymorphism (SNPs) with loss of activity CETP is associated with increased HDL-C, reduced LDL-C, and cardiovascular risk. In animal studies, mostly in rabbits, which have similar CETP activity to humans, inhibition of CETP through antisense oligonucleotides reduced aortic arch atherosclerosis. Concerning this notion, inhibiting the CETP is considered as a promise approach to reduce cardiovascular events, and several CETP inhibitors have been recently studied as a cholesterol modifying agent to reduce cardiovascular mortality in high risk cardiovascular disease patients. However, in Phase III cardiovascular outcome trials, three CETP inhibitors, named Torcetrapib, Dalcetrapib, and Evacetrapib, did not provide expected cardiovascular benefits and failed to improve outcomes of patient with cardiovascular diseases (CVD). Although REVEAL trail has recently shown that Anacetrapib could reduce major coronary events, it was also shown to induce excessive lipid accumulation in adipose tissue; thereby, the further regulatory approval will not be sought. On the other hand, growing evidence indicated that the function of CETP inhibitors on modulating the cardiovascular events are determined by correlated single nucleotide polymorphism (SNP) in the ADCY9 gene. However, the underlying mechanisms whereby CETP inhibitors interact with the genotype are not yet elucidated, which could potentially be related to the genotype-dependent cholesterol efflux capacity of HDL particles. In the present review, we summarize the current understanding of the functions of CETP and the outcomes of the phase III randomized controlled trials of CETP inhibitors. In addition, we also put forward the implications from results of the trials which potentially suggest that the CETP

inhibitors could be a promising precise therapeutic medicine for CVD based on genetic background.

[26] *Heijl C, Kahn F, Edsfeldt A et al.* **Carotid Plaque Morphology is Similar in Patients with Reduced and Normal Renal Function**. Clinical Medicine Insights. Cardiology 2020; 14:1179546820951793.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32922111
ABSTRACT
BACKGROUND: Chronic Kidney Disease (CKD) is associated with an increased risk for cardiovascular events such as stroke. However, it is still unclear if decreased kidney function is associated with a vulnerable atherosclerotic plaque phenotype. To explore if renal function was associated with carotid plaque vulnerability we analyzed carotid plaques obtained at surgery from the Carotid Plaque Imaging Project (CPIP). METHODS: Patients were enrolled through the CPIP cohort. The indication for surgery was plaques with stenosis >70%, associated with ipsilateral symptoms or plaques with stenosis >80% not associated with symptoms. Transversal sections from the most stenotic plaque region were analyzed for connective tissue, calcium, lipids, macrophages, intraplaque hemorrhage, and smooth muscle cells. Homogenates were analyzed for collagen and elastin. RESULTS: Carotid endarterectomy specimens from 379 patients were obtained. The median GFR was 73 ml/min/1.73 m(2). Plaque characteristics showed no significant association with eGFR, neither when eGFR was divided in CKD groups nor when eGFR was handled as a continuous variable and adjusting for other known risk factors (ie, age, diabetes, hypertension, and smoking). CONCLUSIONS: The higher risk of cardiovascular disease such as stroke in CKD is not associated with increased plaque vulnerability and other factors have to be sought.

[27] *Al-Leswas D, Eltweri AM, Chung WY et al.* **Intravenous omega-3 fatty acids are associated with better clinical outcome and less inflammation in patients with predicted severe acute pancreatitis: A randomised double blind controlled trial**. Clinical nutrition (Edinburgh, Scotland) 2020; 39:2711-2719.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32921364
ABSTRACT
BACKGROUND AND AIMS: Omega-3 fatty acids (FA) can ameliorate the hyper-inflammatory response that occurs in conditions such as severe acute pancreatitis (SAP) and this may improve clinical outcome. We tested the hypothesis that parenteral omega-3 FA from a lipid emulsion that includes fish oil could be beneficial in patients with predicted SAP by reducing C-reactive protein (CRP) concentration (primary outcome), and modulating the inflammatory response and improving clinical outcome (secondary outcomes). METHODS: In a phase II randomized double-blind single-centre controlled trial, patients with predicted SAP were randomised to receive a daily infusion of fish oil containing lipid emulsion (Lipidem® 20%, BBraun) for 7 days (n = 23) or a daily infusion of a lipid emulsion without fish oil (Lipofundin® MCT 20%, BBraun) (n = 22). RESULTS: On admission, both groups had comparable pancreatitis predicted severity and APACHE II scores. Administration of fish oil resulted in lower total blood leukocyte number (P = 0.04), CRP (P = 0.013), interleukin-8 (P = 0.05) and intercellular adhesion molecule 1 (P = 0.01) concentrations, multiple organ dysfunction score, sequential organ failure assessment score (P = 0.004), early warning score (P = 0.01), and systemic inflammatory response syndrome (P = 0.03) compared to the control group. The fish

oil group had fewer new organ failures (P = 0.07), lower critical care admission rate (P = 0.06), shorter critical care stay (P = 0.03) and shorter total hospital stay (P = 0.04). CONCLUSIONS: It is concluded that intravenous administration of a fish oil containing lipid emulsion, a source of omega-3 FA, improves clinical outcomes in patients with predicted SAP, benefits that may be linked to reduced inflammation. CLINICALTRIALS. GOV NUMBER: NCT01745861. EU CLINICAL TRIALS REGISTER: EudraCT (2010-018660-16).

[28] *Katzmann JL, Sorio-Vilela F, Dornstauder E et al.* **Non-statin lipid-lowering therapy over time in very-high-risk patients: effectiveness of fixed-dose statin/ezetimibe compared to separate pill combination on LDL-C**. Clinical research in cardiology : official journal of the German Cardiac Society 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32949286
ABSTRACT
BACKGROUND: Many patients at very-high atherosclerotic cardiovascular disease risk do not reach guideline-recommended targets for LDL-C. There is a lack of data on real-world use of non-statin lipid-lowering therapies (LLT) and little is known on the effectiveness of fixed-dose combinations (FDC). We therefore studied prescription trends in oral non-statin LLT and their effects on LDL-C. METHODS: A retrospective analysis was conducted of electronic medical records of outpatients at very-high cardiovascular risk treated by general practitioners (GPs) and cardiologists, and prescribed LLT in Germany between 2013 and 2018. RESULTS: Data from 311,242 patients were analysed. Prescriptions for high-potency statins (atorvastatin and rosuvastatin) increased from 10.4% and 25.8% of patients treated by GPs and cardiologists, respectively, in 2013, to 34.7% and 58.3% in 2018. Prescription for non-statin LLT remained stable throughout the period and low especially for GPs. Ezetimibe was the most prescribed non-statin LLT in 2018 (GPs, 76.1%; cardiologists, 92.8%). Addition of ezetimibe in patients already prescribed a statin reduced LDL-C by an additional 23.8% (32.3 ± 38.4 mg/dL), with a greater reduction with FDC [reduction 28.4% (40.0 ± 39.1 mg/dL)] as compared to separate pills [19.4% (27.5 ± 33.8 mg/dL)]; p < 0.0001. However, only a small proportion of patients reached the recommended LDL-C level of < 70 mg/dL (31.5% with FDC and 21.0% with separate pills). CONCLUSIONS: Prescription for high-potency statins increased over time. Non-statin LLT were infrequently prescribed by GPs. The reduction in LDL-C when statin and ezetimibe were prescribed in combination was considerably larger for FDC; however, a large proportion of patients still remained with uncontrolled LDL-C levels.

[29] *Lee HY, Han KH, Chung WB et al.* **Safety and Efficacy of Pitavastatin in Patients With Impaired Fasting Glucose and Hyperlipidemia: A Randomized, Open-Labeled, Multicentered, Phase IV Study**. Clinical therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32921501
ABSTRACT
PURPOSE: Although the role of high-intensity lipid-lowering therapy in cardiovascular protection has broadened, concerns still exist about new-onset diabetes mellitus (NODM), especially in vulnerable patients. This study aimed to compare the effect of high-dose (4 mg/d) and usual dose (2 mg/d) pitavastatin on glucose metabolism in patients with hyperlipidemia and impaired fasting glucose (IFG). METHODS: In this 12-month study, glucose tolerance and lipid-lowering efficacy of high-dose pitavastatin (4 mg [study group]) was compared with that of usual dose pitavastatin (2 mg [control group]) in patients with hyperlipidemia and IFG. The

primary end point was the change of glycosylated hemoglobin (HbA(1c)) after 24 weeks of treatment. The secondary end points were as follows: (1) NODM within 1 year after treatment, (2) change of lipid parameters, (3) changes of adiponectin, and (4) change of blood glucose and insulin levels. FINDINGS: Of the total 417 patients screened, 313 patients with hypercholesterolemia and IFG were randomly assigned into groups. The mean (SD) change in HbA(1c) was 0.06% (0.20%) in the study group and 0.03% (0.22%) in the control group (P = 0.27). Within 1 year, 27 patients (12.3%) developed NODM, including 12 (10.6%) of 113 patients in the study group and 15 (14.2%) of 106 in the control group (P = 0.43). The study group had a significantly higher reduction of total cholesterol and LDL-C levels and a higher increase in apolipoprotein A1/apolipoprotein B ratio (0.68 [0.40] vs 0.51 [0.35], P < 0.01). IMPLICATIONS: The high-dose pitavastatin therapy did not aggravate glucose metabolism compared with the usual dose therapy. Moreover, it had a better effect on cholesterol-lowering and apolipoprotein distribution in the patients with hyperlipidemia and IFG.

[30] *Penson PE, Banach M*. **The Role of Nutraceuticals in the Optimization of Lipid-Lowering Therapy in High-Risk Patients with Dyslipidaemia**. Current atherosclerosis reports 2020; 22:67.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32945980
ABSTRACT
PURPOSE OF REVIEW: We aimed to summarize recent guidelines, position papers, and high-quality clinical research relating the use of nutraceuticals in the management of individuals at high risk of atherosclerotic cardiovascular disease. RECENT FINDINGS: It is essential that individuals at high risk of cardiovascular disease receive guideline-directed evidence-based therapies to reduce their risk of morbidity and mortality from cardiovascular events. Compared with conventional therapeutics, nutraceuticals have undergone relatively little investigation in randomized controlled trials. Thus, recommendations for nutraceuticals in international guidelines are rare, and nutraceuticals should not be used preferentially in place of statins. Nevertheless, recent position papers from the International Lipid Expert Panel and clinical evidence from studies of triglyceride reduction by polyunsaturated fatty acid administration demonstrate that nutraceuticals do have an important role in optimizing therapy in individuals at high risk of cardiovascular disease. Roles for nutraceuticals include as follows: (1) managing residual risk associated with lipids other than low-density lipoprotein cholesterol (LDL-C); (2) managing non-lipid-mediated residual risk; (3) optimizing LDL-C treatment in statin intolerance; (4) optimizing LCL-C treatment when add-on therapies for statins are not available; (5) as adjuncts to lifestyle for individuals at high lifetime risk of atherosclerotic cardiovascular disease (ASCVD). The strength of evidence for each of these applications is variable. In addition to guideline-directed therapeutics, nutraceuticals may have roles in optimizing preventative therapy and targeting residual risk in individuals at high risk of ASCVD. Application of Good Manufacturing Practice and randomized controlled trials when producing and evaluating nutraceuticals will expand the armoury of evidence-based agents for the prevention of ASCVD.

[31] *Pokrovsky SN, Afanasieva OI, Ezhov MV*. **Therapeutic Apheresis for Management of Lp(a) Hyperlipoproteinemia**. Current atherosclerosis reports 2020; 22:68.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32945973
ABSTRACT

PURPOSE OF REVIEW: High lipoprotein(a) (Lp(a)) level is an independent cardiovascular risk factor with higher prevalence among patients with atherosclerotic cardiovascular disease (ASCVD). The actual problem is that most currently available lipid-lowering drugs are unable to abolish Lp(a) pathogenicity. Lipoprotein apheresis (LA) is an effective method for elimination of atherogenic lipoproteins, but it is approved only in some countries for treatment of elevated Lp(a) level in the presence of progressive ASCVD. In recent years, new studies on LA were published and the purpose of this review is to present the information on optimal management of Lp(a) hyperlipoproteinemia by LA in the modern era. RECENT FINDINGS: Most clinical studies designed to treat Lp(a) hyperlipoproteinemia with different LA systems are small in size but demonstrate that the elimination of Lp(a) from bloodstream leads to reduction of inflammatory and prothrombotic process in a few months and to atherosclerotic plaques regression in 1.5 years. Treatment with LA for 2 to 5 years in terms of clinical trials and in real-world setting provides further evidence that Lp(a) reduction by 60-80% is associated with proportional decreasing of rate and risk of cardiovascular events. Specific Lp(a) apheresis is the only possible method that solely targets Lp(a). In most countries, non-specific LA is used for treatment Lp(a) hyperlipoproteinemia in very high-risk subjects with progressive ASCVD. PCSK9 inhibitors have only modest effect on significantly elevated Lp(a), whereas large population-based studies requested sustained and prolonged reduction of Lp(a) levels by 50-100 mg/dL to gain proportional decreasing of major adverse cardiovascular events.

[32] *Evangelista A, Moral S*. **Penetrating atherosclerotic ulcer**. Current opinion in cardiology 2020; 35:620-626.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32925190
ABSTRACT
PURPOSE OF REVIEW: Penetrating aortic ulcer (PAU) is defined as ulceration of an aortic atherosclerotic plaque penetrating through the internal elastic lamina into the media. With the advances in imaging techniques, the differential diagnosis between PAU and other aortic ulcers remains a challenge. This review aims to summarize the latest insight into PAU, based on clinical context and the newest imaging characteristics, to aid treatment decision-making. RECENT FINDINGS: Most PAUs are asymptomatic and do not require urgent invasive treatment. Nevertheless, when PAU leads to an acute aortic syndrome, emergency invasive therapy is recommended. A differential diagnosis with other lesions, such as ulcerated plaques or intimal disruptions within the context of an aortic intramural hematoma, is required as the risk of complications and management differ. Imaging technique plays a pivotal role in the correct diagnosis of aortic ulcers. SUMMARY: The differential diagnosis of PAU with other aortic ulcers based on clinical and imaging technique information is mandatory as it may imply different prognosis and management. This diagnosis is particularly important when PAU is the cause of acute aortic syndromes as urgent invasive treatment should be recommended.

[33] *Hirigo AT, Teshome T*. **The magnitude of undiagnosed diabetes and Hypertension among adult psychiatric patients receiving antipsychotic treatment**. Diabetology & metabolic syndrome 2020; 12:79.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32944092
ABSTRACT
BACKGROUND: Patients with severe mental illness (SMI) are at increased risk of developing non-communicable diseases that could cause significantly lower life expectancy when

compared to the general population. This study aimed to assess the magnitude and predictors of undiagnosed type-2 diabetes and hypertension among adult patients with SMI on antipsychotic treatments. METHODS: A hospital-based cross-sectional study was conducted on 237 psychiatric patients from January to June 2019 at Hawassa University Comprehensive Specialized Hospital, Hawassa, Southern Ethiopia. All relevant information was collected using a structured interviewer-administered questionnaire with a systematic random sampling technique. A total of 4-5 mL of overnight fasting venous blood was collected from each patient. Serum lipid profiles and fasting blood sugar (FBS) were measured using the A25™ BioSystem Random Access chemistry analyzer. To identify predictors of hyperglycemia and raised blood pressure, multiple linear regression analysis was done using SPSS version 23. Statistical significance was set at p value < 5%. RESULTS: From 247 patients with SMI approached, 237 (58.2% male and 41.8% females) were take part in the study giving a response rate of 95.9%. The overall 31.2% (95%CI: 24.1-37.6) and 27.8% (95%CI: 23.2-33.4) of patients had hyperglycemia and raised BP. The magnitude of prediabetes and type-2 diabetes was 24.9% (95%CI:19.4-30.4), and 6.3% (95% CI: 3.4-10.1), respectively. While the magnitude of prehypertension and hypertension was 23.2% (95%CI: 17.3-29.5) and 4.6% (95%CI: 2.1-8.0), respectively. In multiple linear regression analyses: age, HDL-cholesterol, physical activity and Triglyceride/HDL-cholesterol ratio were positively correlated with FBS. While, HDL-cholesterol, waist circumference, physical activity, total cholesterol/HDL-c ratio, and body mass index were positively correlated with systolic and diastolic blood pressures. CONCLUSION: The findings indicate a need to assess blood glucose and blood pressure at baseline before the commencement of any antipsychotic therapy and during therapeutic follow up to manage any increasing trends. Moreover, close monitoring of patients with severe mental illness on antipsychotic therapy is exclusively recommended.

[34] *Marrs JC, Anderson SL*. **Bempedoic acid for the treatment of dyslipidemia**. Drugs in context 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32922503

ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death worldwide and one key factor associated with the increased CVD risk is dyslipidemia. Statin therapy remains the first-line treatment to manage dyslipidemia, yet many patients do not achieve optimal low-density lipoprotein-cholesterol (LDL-C) levels even after taking moderate- or high-intensity statins; therefore, additional, non-statin therapy is often needed. Bempedoic acid is a prodrug that, once activated, decreases LDL-C levels by the inhibition of adenosine triphosphate citrate lyase in the liver. Five clinical trials have demonstrated the safety and efficacy of bempedoic acid and the bempedoic acid/ezetimibe combination in lowering LDL-C in patients with atherosclerotic CVD and heterozygous familial hypercholesterolemia and also in high-risk primary prevention, and statin-intolerant patients. Bempedoic acid has been demonstrated to lower LDL-C levels by 15-25% in clinical trials and up to 38% when combined with ezetimibe. In 2020, the FDA approved bempedoic acid. Furthermore, the combination of bempedoic acid with ezetimibe is FDA approved for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic CVD who require additional LDL-C lowering after maximally tolerated statin therapy. The ongoing CLEAR OUTCOMES trial aims to evaluate whether bempedoic acid can reduce cardiovascular events in patients with statin

intolerance and results will be available in the next 3 years. This outcomes trial will be pivotal for determining the role of bempedoic acid in the non-statin lipid-lowering armamentarium.

[35] *Donzelli A, Giudicatti G, Duca P*. **[New European guidelines for the management of dyslipidaemias: their aggressiveness is not legitimated by current evidence]**. Epidemiol Prev 2020; 44:308-312.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32921038
ABSTRACT
Le linee guida 2019 delle Società europee di cardiologia e dell'aterosclerosi sulla gestione delle dislipidemie hanno aumentato l'aggressività diagnostico-terapeutica e non distinguono prevenzione primaria e secondaria, con parziale eccezione per gli ultra75enni. Raccomandano nuovi target di cLDL: per pazienti a rischio molto alto si raccomanda una riduzione a <55 mg/dl e >=50% rispetto al basale; per pazienti a rischio alto una riduzione a <70 mg/dl e >=50% del basale; per pazienti a rischio moderato una riduzione a <100 mg/dl; per pazienti a rischio basso una riduzione a <116 mg/dl. In base alle carte SCORE e ai dati di mortalità cardiovascolare in Italia, quasi tutti i maschi dai 70 anni e le donne dai 70-75 anni risulterebbero ad alto rischio per solo effetto dell'età. Anche quasi tutti i 60enni sarebbero a rischio moderato, con target di cLDL <100, e spesso necessità di aggiungere costosi ipolipemizzanti per chi già assume statine. Le prove supportano ben poco tale aggressività. Infatti, anche negli studi randomizzati controllati (RCT) i benefici su esiti cardiovascolari non fatali subiscono esagerazioni sistematiche, quello meno distorto e di maggior interesse per gli assistiti è la mortalità totale. Questa, con terapie ipocolesterolemizzanti più intensive, non si è ridotta nelle metanalisi di RCT con pazienti con cLDL tra 80 e <100 mg/dl al basale; con inibitori di PCSK9, pazienti con questi valori mostrano persino tendenza all'aumento della mortalità totale. Dunque, abbassare il cLDL a <80 mg/dl può non giovare neppure ad anziani coronaropatici. A oggi, ciò vale ancora di più per anziani nella popolazione generale, in cui una revisione sistematica di studi di coorte ha mostrato relazioni nulle o più spesso inverse tra cLDL e mortalità. Le nuove linee guida europee forzano le prove disponibili, trascurano il principio di precauzione e non possono esser base per un equo consenso informato.

[36] *Truong TH, Do DL, Kim NT et al.* **Genetics, Screening, and Treatment of Familial Hypercholesterolemia: Experience Gained From the Implementation of the Vietnam Familial Hypercholesterolemia Registry**. Frontiers in genetics 2020; 11:914.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32922439
ABSTRACT
Familial hypercholesterolemia (FH) is underdiagnosed and undertreated in a majority of the low- and middle-income countries. FH registries could prove useful in bridging the knowledge gaps, supporting genetic and clinical research, and improving health-care planning and patient care. Here, we report the first usage experience of the Vietnam FH (VINAFH) Registry. The VINAFH Registry was established in 2016 as a long-term database for prospective cohorts. FH patients were detected based on the opportunistic and cascade screening. Diagnosis of FH was assessed using the Dutch Lipid Clinic Network criteria, plasma levels of low-density lipoprotein (LDL) cholesterol, and genetic testing. To date, a total of 130 patients with FH have been registered, with 48 index cases and 82 relatives. Of the 130 patients, 8 were homozygous FH patients and 38 were children. Of FH individuals, 46.7% was confirmed by genetic testing: 61 patients (96.8%) carried the LDLR mutation (c.681C > G, c.1427C > G,

c.1187-?_2140 ± ?del, c.2529_2530delinsA), and two patients (3.2%) carried the PCSK9 (protein convertase subtilisin/kexin type 9) mutation (c.42_43insTG). The c.2529_2530delinsA mutation detected in this study is novel and reported only in the Vietnamese population. However, only 53.8% of FH patients were followed up post diagnosis, and only 15.3% of these were approved for lipid-lowering therapy and specialized care. Notably, factors such as knowledge about FH in patients and/or guardians of FH children and support of primary care physicians affected patient participation with respect to treatment strategies and follow-up. Genetic identification, screening, and treatment of FH were feasible in Vietnam. The VINAFH Registry significantly contributed to the formation of the government agencies legislative acts that established the importance of FH as a socially and medically important disease requiring appropriate management strategies. Other low- and middle-income countries could, thus, use the VINAFH Registry model as a reference to establish programs for FH management according to the current status.

[37] *Bergmeijer TO, Yasmina A, Vos GJA et al.* **Effect of CYP3A4*22 and PPAR-α Genetic Variants on Platelet Reactivity in Patients Treated with Clopidogrel and Lipid-Lowering Drugs Undergoing Elective Percutaneous Coronary Intervention**. Genes 2020; 11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32932966
ABSTRACT
This study aims to determine whether genetic variants that influence CYP3A4 expression are associated with platelet reactivity in clopidogrel-treated patients undergoing elective percutaneous coronary intervention (PCI), and to evaluate the influence of statin/fibrate co-medication on these associations. A study cohort was used containing 1124 consecutive elective PCI patients in whom CYP3A4*22 and PPAR-α (G209A and A208G) SNPs were genotyped and the VerifyNow P2Y(12) platelet reactivity test was performed. Minor allele frequencies were 0.4% for CYP3A4*22/*22, 6.8% for PPAR-α G209A AA, and 7.0% for PPAR-α A208G GG. CYP3A4*22 was not associated with platelet reactivity. The PPAR-α genetic variants were significantly associated with platelet reactivity (G209A AA: -24.6 PRU [-44.7, -4.6], p = 0.016; A208G GG: -24.6 PRU [-44.3, -4.8], p = 0.015). Validation of these PPAR-α results in two external cohorts, containing 716 and 882 patients, respectively, showed the same direction of effect, although not statistically significant. Subsequently, meta-analysis of all three cohorts showed statistical significance of both variants in statin/fibrate users (p = 0.04 for PPAR-a G209A and p = 0.03 for A208G), with no difference in statin/fibrate non-users. In conclusion, PPAR-α G209A and A208G were associated with lower platelet reactivity in patients undergoing elective PCI who were treated with clopidogrel and statin/fibrate co-medication. Further research is necessary to confirm these findings.

[38] *Wang M, Liu J, Bellows BK et al.* **Impact of China's Low Centralized Medicine Procurement Prices on the Cost-Effectiveness of Statins for the Primary Prevention of Atherosclerotic Cardiovascular Disease**. Global heart 2020; 15:43.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32923337
ABSTRACT
BACKGROUND: Statin medications reduce the risk of atherosclerotic cardiovascular disease (ASCVD). China's new central government medicine procurement policy lowered statin prices by five-fold or more, which may impact the cost-effectiveness of statin therapy. OBJECTIVE: To explore the impact of China's 2019 centralized medicine procurement policy on the cost-

effectiveness of statins treatment for primary ASCVD prevention. METHODS: A microsimulation decision tree analytic model was built using individual participant data from ASCVD-free adults aged 35-64 years (n = 21,265) in the China Multi-provincial Cohort Study. ASCVD incidence, costs (2019 Int$), and quality-adjusted life years (QALYs) over a 10-year period from health-care sector and societal perspectives were estimated. Effect and cost-effectiveness of low-dose statins (equivalent potency regimens of simvastatin 20 mg/day, atorvastatin 10 mg/day, or rosuvastatin 5 mg/day) and moderate-dose (double low dose) statins therapy were simulated. The incremental cost-effectiveness ratio (ICER) of statin treatment was compared with no treatment by category of 10-year ASCVD risk. New lower prices of statins were from the centralized procurement policy bid-winning announcement file. One-way and probabilistic sensitivity analyses quantified model uncertainty. RESULTS: Low-dose statins interventions reduced 10-year ASCVD incidence by 4.1%, 9.7%, and 15.5% among people with low, moderate, and high risk comparing to no treatment. Lowering statin prices to the 2019 central government procurement policy level could lower the ICER of low-dose statins treatment for high-risk people from Int$ 141,000 to Int$ 51,300 per QALY gained from health-care sector perspective. Moderate-dose statin treatment lowered the ICER compared with the low-dose statins treatment in each ASCVD risk category (Int$ 43,100 vs. Int$ 51,300 per QALY gained from the health-care sector perspective for high risk people). Cost-effectiveness improved progressively with increased baseline ASCVD risk. CONCLUSION: Implementing low central government prices will substantially improve the cost-effectiveness of statins for primary ASCVD prevention in 35-64-year-old Chinese adults.

[39] *Meng L, Liu X, Yu H et al.* **Incidence and Predictors of Neoatherosclerosis in Patients with Early In-Stent Restenosis Determined Using Optical Coherence Tomography**. Int Heart J 2020; 61:872-878.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32921669

ABSTRACT

In-stent restenosis (ISR) still exists after drug-eluting stent (DES) implantation, even up to one year. The incidence and risk factors for neoatherosclerosis in patients with early ISR have not yet been elucidated. Here, we used optical coherence tomography (OCT) to evaluate the incidence and predictors of neoatherosclerosis in patients with early ISRs.OCT was performed on ISR lesions in 185 patients in order to detect neoatherosclerosis. The median follow-up was 180 days, and neoatherosclerosis was detected in 37% of early ISR lesions. According to the presence of neoatherosclerosis, patients with ISR were divided into two groups: neoatherosclerosis (group A, n = 69) and non-neoatherosclerosis (group B, n = 116) groups.The risk factors were similar, except for hypercholesterolemia. Moreover, the tissue characteristics were not significantly different between patients with and without neoatherosclerosis. Follow-up low-density lipoprotein-cholesterol (LDL-C) levels were divided into three grades (LDL < 70 mg/dL, 70 mg/dL≤ LDL < 100 mg/dL, and LDL ≥ 100 mg/dL). The incidence of neoatherosclerosis was significantly lower (23% versus 57%, P < 0.0001) in the LDL < 70 mg/dL group. There was no significant difference in the incidence of neoatherosclerosis in patients with lipid levels between 70 and 100 mg/dL (P = 0.53). However, neoatherosclerosis was significantly more common in patients with a follow-up LDL-C level > 100 mg/dL (45% versus 15%, P < 0.0001).In patients with early ISR lesions, the LDL-C levels may be related to the formation and progression of early neoatherosclerosis, and poor

LDL-C control may be a risk factor for the occurrence of early-stage neoatherosclerosis following DES implantation.

[40] *Boccara F, Rosenson RS*. **Reply: Role of Ezetimibe in the Current Era in Treating Dyslipidemia in HIV-Infected Patients**. Journal of the American College of Cardiology 2020; 76:1503-1504.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32943170
ABSTRACT

[41] *Singh A, Mittal S, Kazimuddin M*. **Role of Ezetimibe in the Current Era in Treating Dyslipidemia in HIV-Infected Patients**. Journal of the American College of Cardiology 2020; 76:1503.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32943169
ABSTRACT

[42] *Jin X, Kim MH, Han KH et al.* **Efficacy and safety of co-administered telmisartan/amlodipine and rosuvastatin in subjects with hypertension and dyslipidemia**. Journal of clinical hypertension (Greenwich, Conn.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32937023
ABSTRACT
Single risk factors, such as hypertension and dyslipidemia, can combine to exacerbate the development and severity of cardiovascular disease. Treatment goals may be more effectively achieved if multiple disease factors are targeted with combination treatment. We enrolled 202 patients who were randomly divided into the following three groups: telmisartan/amlodipine 80/5 mg + rosuvastatin 20 mg, telmisartan 80 mg + rosuvastatin 20 mg, and telmisartan/amlodipine 80/5 mg. The primary efficacy variables were changes from baseline in mean sitting systolic blood pressure (MSSBP) between telmisartan/amlodipine 80/5 mg + rosuvastatin 20 mg and telmisartan 80 mg + rosuvastatin 20 mg at 8 weeks, and the percent changes from baseline in low-density lipoprotein (LDL) cholesterol between telmisartan/amlodipine 80/5 mg + rosuvastatin 20 mg and telmisartan/amlodipine 80/5 mg at 8 weeks. The secondary efficacy variables were changes in MSSBP, mean sitting diastolic blood pressure (MSDBP), LDL cholesterol and other lipid levels at 4 weeks and 8 weeks, as well as observed adverse events during follow-up. There were no significant differences between the three groups in demographic characteristics and no significant difference among the three groups in terms of baseline characteristics for the validity evaluation variables. The mean overall treatment compliance in the three groups was, respectively, 98.42%, 96.68%, and 98.12%, indicating strong compliance for all patients. The Least-Square (LS) mean (SE) for changes in MSSBP in the two (telmisartan/amlodipine 80/5 mg + rosuvastatin 20 mg and telmisartan 80 mg + rosuvastatin 20 mg) groups were -19.3 (2.68) mm Hg and -6.69 (2.76) mm Hg. The difference between the two groups was significant (-12.60 (2.77) mm Hg, 95% CI -18.06 to -7.14, P < .0001). The LS Mean for the percent changes from baseline in LDL cholesterol in the two (telmisartan/amlodipine 80/5 mg + rosuvastatin 20 mg and telmisartan/amlodipine 80/5 mg) groups were -52.45 (3.23) % and 2.68 (3.15) %. The difference between the two groups was significant (-55.13 (3.20) %, 95% CI -61.45 to -48.81, P < .0001). There were no adverse events leading to discontinuation or death. Combined administration of telmisartan/amlodipine 80/5 mg and rosuvastatin 20 mg for the treatment of

hypertensive patients with dyslipidemia significantly reduces blood pressure and improves lipid control. ClinicalTrials.gov identifier: NCT03067688.

[43] *Roth EM, Kastelein JJP, Cannon CP et al.* **Pharmacodynamic relationship between PCSK9, alirocumab, and LDL-C lowering in the ODYSSEY CHOICE I trial**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32928709
ABSTRACT
BACKGROUND: The ODYSSEY CHOICE I study (NCT01926782) evaluated alirocumab 300 mg every 4 weeks (Q4W) in patients with hypercholesterolemia receiving maximally tolerated statin or no statin. OBJECTIVE: The objective of the study was to assess the relationship between alirocumab, proprotein convertase subtilisin/kexin type 9 (PCSK9), and low-density lipoprotein cholesterol (LDL-C) concentrations with the CHOICE I alirocumab dosing regimen. METHODS: This analysis included 803 patients (547 statin-treated, 256 without statin) who were randomized to alirocumab 300 mg Q4W, alirocumab 75 mg every 2 weeks (Q2W), or placebo. 300 mg Q4W and 75 mg Q2W doses were adjusted to 150 mg Q2W at Week 12 if Week 8 LDL-C was >70 or >100 mg/dL, depending on cardiovascular risk, or if LDL-C reduction was <30% from baseline. RESULTS: Most patients remained on 300 mg Q4W without dose adjustment as they achieved study-defined LDL-C goals at Week 8 (statin-treated: 80.7%; no statin: 85.3%). LDL-C was reduced by 60.5%-71.9% over Weeks 20-24 in patients on 300 mg Q4W and 57.2%-63.0% in patients with dose adjustment from 300 mg Q4W to 150 mg Q2W. Statin-treated patients had higher cardiovascular risk as well as higher free PCSK9 and lower alirocumab concentrations (vs no statin), suggesting increased target-mediated clearance. Regardless of statin status, the most common adverse events in alirocumab-treated patients were injection-site reaction and headache. CONCLUSIONS: Data provide further insight on alirocumab's mode of action in terms of relationship between alirocumab, PCSK9, and LDL-C, and disease severity, and support the use of alirocumab 300 mg Q4W as an efficacious dosing regimen for clinically meaningful LDL-C reductions.

[44] *Kaddoura R, Orabi B, Salam AM*. **Efficacy and safety of PCSK9 monoclonal antibodies: an evidence-based review and update**. Journal of drug assessment 2020; 9:129-144.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32939318
ABSTRACT
OBJECTIVE: Treatment of dyslipidemia lowers cardiovascular (CV) risk. Although statin use is a cornerstone therapy, many patients are not achieving their risk-specific low-density lipoprotein cholesterol (LDL-C) goals. The proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies have been extensively studied as lipid-lowering therapy (LLT). Herein, we present an updated evidence-based review of the efficacy and safety of PCSK9 monoclonal antibodies in the treatment of familial and non-familial hypercholesterolemia. METHODS: PubMed database was searched to review Phase III studies on PCSK9 monoclonal antibodies. Then, the US National Institutes of Health Registry and the WHO International Clinical Trial Registry Platform were searched to identify and present the ongoing research. RESULTS: PCSK9 monoclonal antibodies were investigated for the treatment of dyslipidemia, as a single therapeutic agent or as an add-on therapy to the traditional LLT. They proved effective and safe in the treatment of familial and non-familial hypercholesterolemia,

and in the prevention of adverse CV events. CONCLUSIONS: The use of PCSK9 monoclonal antibodies in the treatment of dyslipidemia is currently recommended to achieve risk-specific LDL-C goal to reduce adverse CV events. Future results of the ongoing research might expand their clinical generalizability to broader patient populations.

[45] *Jakimovski D, Zivadinov R, Dwyer MG et al.* **High density lipoprotein cholesterol and apolipoprotein A-I are associated with greater cerebral perfusion in multiple sclerosis**. J Neurol Sci 2020; 418:117120.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32947088
ABSTRACT
BACKGROUND: The pathophysiological mechanisms underlying the associations of multiple sclerosis (MS) neurodegeneration serum cholesterol profiles is currently unknown. OBJECTIVE: To determine associations between lipid profile measures and cerebral perfusion-based indices in MS patients. METHODS: Seventy-seven MS patients underwent 3 T MRI. Cerebral blood volume (CBV), time-to-peak (TTP) and mean transit time (MTT) measures were computed from dynamic susceptibility contrast (DSC) perfusion-weighted imaging (PWI) for normal-appearing brain tissue (NABT), GM, cortex, deep gray matter (DGM) and thalamus. Total cholesterol, low and high-density lipoprotein cholesterol (LDL-C and HDL-C) and the apolipoproteins (Apo), ApoA-I, ApoA-II, ApoB, ApoC-II and ApoE levels were measured in plasma. Age and body mass index (BMI)-adjusted correlations were used to assess the associations between PWI and lipid profile measures. RESULTS: Higher HDL-C levels were associated with shorter MTT, which are indicative of greater perfusion, in NABT ($p = 0.012$), NAWM ($p = 0.021$), GM ($p = 0.009$), cortex ($p = 0.014$), DGM $p = 0.015$; and thalamus $p = 0.015$). The HDL-C-associated apolipoproteins, ApoA-I and ApoA-II, were associated with shorter MTT of the same brain regions (all $p < 0.028$). HDL-C and ApoA-I levels were also associated with shorter TTP, indicative of faster cerebral blood delivery. ApoC-II was associated with lower nCBV of the GM and cortex ($p = 0.035$ and $p = 0.014$, respectively). CONCLUSION: The HDL pathway is associated with better global brain perfusion and faster cerebral blood delivery as measured by shorter MTT and TTP, respectively. ApoC-II may be associated with lower cortical and DGM perfusion.

[46] *Barrons R, Woods JA, Humphries R*. **Statin Associated Autoimmune Myopathy**. Journal of pharmacy practice 2020:897190020958223.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32924771
ABSTRACT
PURPOSE: A case of delayed statin associated autoimmune myopathy (SAAM) is presented along with review of clinical findings and treatment strategies. SUMMARY: A 54 year old male presented with proximal extremity weakness, difficulty ambulating, and dysphagia. Symptoms began when restarting atorvastatin 40 mg daily for a recent NSTEMI, following 10 years of statin use, interrupted after diagnosis of NASH. Relevant labs included CK of 13,618 IU/L, ALT/ AST of 568/407 IU/L, while additional liver, renal, and toxicology tests were normal. Following treatment response to prednisone 40 mg daily for 3 days, outpatient testing for anti-HMGCR antibodies was ordered.Twelve days from discharge, the patient was readmitted for myalgia and dysphagia, CK = 6042 IU/L, ALT/AST = 360/112 IU/L, and positive anti-HMGCR antibodies. Newly diagnosed with SAAM, symptoms improved with methylprednisolone and intravenous immunoglobulin (IVIG), continuing outpatient as daily prednisone and monthly

IVIG. Four days later, the patient relapsed with worsened weakness and dysphagia, CK = 5812 IU/L, and ALT/AST = 647/337 IU/L. After response to methylprednisolone and rituximab, the patient was discharged on a corticosteroid taper, biweekly rituximab, and monthly IVIG. Two weeks later, a final admission involved a syncopal episode and fall, with a CK = 1461 IU/L. Treatment included IVIG, rituximab, and corticosteroid taper, which lead to remission for greater than 6 months. CONCLUSION: Statin associated autoimmune myopathy occurred when restarting atorvastatin, following 10 years of statin use. Clinical findings and positive anti-HMGCR antibodies confirmed the diagnosis. Recurrent relapses required triple combination therapy including addition of rituximab to achieve remission.

[47] *Guijarro C, Civeira F, Masana L*. **Genetic Confirmation of Monogenic Familial Hypercholesterolemia Advises a More Intensive Lipid-Lowering Approach**. JAMA cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32936217
ABSTRACT

[48] *Trinder M, Brunham LR*. **Genetic Confirmation of Monogenic Familial Hypercholesterolemia Advises a More Intensive Lipid-Lowering Approach-Reply**. JAMA cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32936211
ABSTRACT

[49] *Lee DY, Yoo SH, Min KP, Park CY*. **Effect of Voluntary Participation on Mobile Health Care in Diabetes Management: Randomized Controlled Open-Label Trial**. JMIR Mhealth Uhealth 2020; 8:e19153.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32945775
ABSTRACT
BACKGROUND: The role of mobile health care (mHealth) in glycemic control has been investigated, but its impact on self-management skills and its psychological aspects have not been studied. OBJECTIVE: We evaluated the efficacy of mHealth-based diabetes self-management education and the effect of voluntary participation on its effects. METHODS: This study was a randomized controlled open-label trial conducted for 6 months at Kangbuk Samsung Hospital. Participants in the control group (n=31) maintained their previous diabetes management strategies. Participants in the intervention group (n=41) additionally received mHealth-based diabetes self-management education through a mobile app and regular individualized feedback from health care professionals. The primary outcome was change in glycated hemoglobin (HbA(1c)) level over 6 months between the 2 groups (intervention versus control) and within each group (at 6 months versus baseline). The secondary outcomes were changes in body mass index, blood pressure, lipid profile, and questionnaire scores (the Korean version of the Summary of Diabetes Self-Care Activities Questionnaire, an Audit of Diabetes Dependent Quality of Life, the Appraisal of Diabetes Scale, and Problem Areas in Diabetes) over 6 months between groups and within each group. RESULTS: A total of 66 participants completed this study. HbA(1c) (P=.04), total cholesterol level (P=.04), and Problem Areas in Diabetes scores (P=.02) significantly decreased; total diet (P=.03) and self-monitoring of blood glucose level scores (P=.01), based on the Summary of Diabetes Self-Care Activities Questionnaire, markedly increased within the intervention group. These

significant changes were observed in self-motivated participants who were recruited voluntarily via advertisements. CONCLUSIONS: mHealth-based diabetes self-management education was effective at improving glycemic control and diabetes self-management skills and lowering diabetes-related distress in voluntary participants. TRIAL REGISTRATION: ClinicalTrials.gov NCT03468283; http://clinicaltrials.gov/ct2/show/NCT03468283.

[50] *Pinato DJ*. **Shifting paradigms in the systemic management of hepatocellular carcinoma**. The lancet. Gastroenterology & hepatology 2020; 5:883-885.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32941832
ABSTRACT

[51] *Yao HT, Hsu YR, Li ML*. **Beverage-Drug Interaction: Effects of Green Tea Beverage Consumption on Atorvastatin Metabolism and Membrane Transporters in the Small Intestine and Liver of Rats**. Membranes (Basel) 2020; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32937767
ABSTRACT
Green tea (GT) beverages are popular worldwide and may prevent the development of many chronic diseases including cardiovascular disease and cancer. To investigate whether the consumption of a GT beverage causes drug interactions, the effects of GT beverage consumption on atorvastatin metabolism and membrane transporters were evaluated. Male rats were fed a chow diet with tap water or the GT beverage for 3 weeks. Then, the rats were given a single oral dose (10 mg/kg body weight (BW)) of atorvastatin (ATV), and blood was collected at various time points within 6 h. The results show that GT consumption increased the plasma concentrations (AUC(0-6h)) of ATV (+85%) and 2-OH ATV (+93.3%). GT also increased the 2-OH ATV (+40.9%) and 4-OH ATV (+131.6%) contents in the liver. Decreased cytochrome P450 (CYP) 3A enzyme activity, with no change in P-glycoprotein expression in the intestine, was observed in rats treated with GT. Additionally, GT increased hepatic CYP3A-mediated ATV metabolism and decreased organic anion transporting polypeptides (OATP) 2 membrane protein expression. There was no significant difference in the membrane protein expression of OATP2B1 and P-glycoprotein in the intestine and liver after the GT treatment. The results show that GT consumption may lower hepatic OATP2 and, thus, limit hepatic drug uptake and increase plasma exposure to ATV and 2-OH ATV.

[52] *Rafiq M, Liaquat A, Saeed N et al.* **Gene expression of thrombomodulin, TNF-α and NF-KB in coronary artery disease patients of Pakistan**. Molecular biology reports 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32930934
ABSTRACT
Thrombomodulin (THBD) is an endothelial surface glycoprotein receptor, having a pivotal role in maintaining laminar blood flow. It functions to protect endothelial integrity by exhibiting anti-coagulation and anti-inflammatory properties thereby playing a key role in cardiovascular disease (CVD) pathology. Cholesterol lowering drugs have shown to alter the anti-inflammatory effects of cytokines. Understanding the molecular aspects of THBD gene and its relation to inflammatory cytokines is important to identify new prognostic and therapeutic targets for the CVD treatments. The present study was conducted to measure the expression of THBD, TNF-α and NF-kB genes in coronary artery disease patients (CAD) in Pakistani population. Lipid profile and BMI was compared both on fifty CAD patients and fifty healthy

individuals. Expression analysis for THBD, TNF-α and NF-kB was carried out using real time PCR. The effect of lipid lowering drugs on cardiometabolic risk variables especially gene expression was analyzed. Our results indicated that the difference in BMI was marginal; however LDL-cholesterol and triglycerides levels in CAD patients were significantly higher than healthy individuals. THBD gene was significantly up-regulated whereas TNF-α and NF-kB were significantly down regulated in CAD individuals. Further exploration revealed that these variations were accounted to the use of statins by the patients. The use of statins by CAD patients up-regulated the mRNA expression of THBD by down-regulation of inflammatory mediators. The enhanced expression of endothelial THBD in response to cholesterol lowering drugs establishes a novel pleiotropic target that can be of clinical significance in thromboembolic and inflammatory disorders.

[53] *Goldberg TE, Huey ED, Devanand DP*. **Association of APOE e2 genotype with Alzheimer's and non-Alzheimer's neurodegenerative pathologies**. Nature communications 2020; 11:4727.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32948752
ABSTRACT
The apolipoprotein E (APOE) gene contains both the major common risk variant for late onset Alzheimer's disease (AD), e4, and the major neuroprotective variant, e2. Here we examine the association of APOE e2 with multiple neurodegenerative pathologies, leveraging the NACC v. 10 database of 1557 brains that included 130 e2 carriers and 679 e4 carriers in order to examine potential neuroprotective effects. For AD-related pathologies of amyloid plaques and Braak stage, e2 had large and highly significant protective effects contrasted with e3/e3 and e4 carriers with odds ratios of about 0.50 for e3 contrasts and 0.10 for e4 contrasts. When we separately examined e2/e4 carriers, risk for AD pathologies was similar to that of e4 carriers, not e2 carriers. For multiple fronto-temporal lobar pathologies and tauopathies, e2 was not significantly associated with pathology. In sum, we found that e2 was associated with large but circumscribed protective effects.

[54] *Okafor LO, Bowyer J, Thaung C et al.* **Orbital involvement of Sitosterolemia**. Orbit 2020:1-5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32942937
ABSTRACT
Sitosterolemia is a rare inherited condition in which plant sterols are stored and deposited in the tissues. Described in 1974 by Battacharyya and Connor, it is characterized by tendon and tuberous xanthomas and a propensity to premature coronary atherosclerosis. We present the first reported case of the disease being manifest in the periorbital region. A 44-year-old man presented with a six-month history of swelling below the left eyebrow overlying the orbital rim, but without displacement of the globe. Magnetic resonance imaging identified a soft tissue mass within the orbit, with subsequent biopsy confirming a xanthogranulomatous process consistent with the diagnosis of sitosterolemia. Management of sitosterolemia aims to reduce plasma plant sterol concentrations which subsequently lowers serum cholesterol reducing the xanthomas and atherosclerotic cardiovascular diseases. This report highlights a rare, under-recognised condition (and indeed the first reporting periocular disease), and the potential dangers if misdiagnosed as hypercholesterolemia.

[55] *Lee HW, Kang WY, Jung W et al.* **Evaluation of the Pharmacokinetic Drug-Drug Interaction between Micronized Fenofibrate and Pitavastatin in Healthy Volunteers**. Pharmaceutics 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32932576
ABSTRACT
Dyslipidemia is a major risk factor for development of atherosclerosis and cardiovascular disease (CVD). Effective lipid-lowering therapies has led to CVD risk reduction. This study evaluated the possible pharmacokinetic interactions between fenofibrate, a peroxisome proliferators-activated receptors α agonist, and pitavastatin, a 3-hydoxy-3-methylglutaryl-coenzyme A reductase inhibitor, in healthy Korean subjects. The study design was an open-label, randomized, multiple-dose, three-period, and six-sequence crossover study with a 10-day washout in 24 healthy volunteers. It had three treatments: 160 mg of micronized fenofibrate once daily for 5 days; 2 mg of pitavastatin once daily for 5 days; and 160 mg of micronized fenofibrate with 2 mg of pitavastatin for 5 days. Serial blood samples were collected at scheduled intervals for up to 48 h after the last dose in each period to determine the steady-state pharmacokinetics of both drugs. Plasma concentrations of fenofibric acid and pitavastatin were measured using a validated high-performance liquid chromatography with the tandem mass spectrometry method. A total of 24 subjects completed the study. Pitavastatin, when co-administered with micronized fenofibrate, had no effect on the C(max,ss) and AUC(τ,ss) of fenofibric acid. The C(max,ss) and AUC(τ,ss) of pitavastatin were increased by 36% and 12%, respectively, when co-administered with fenofibrate. Combined treatment with pitavastatin and micronized fenofibrate was generally well tolerated without serious adverse events. Our results demonstrated no clinically significant pharmacokinetic interactions between micronized fenofibrate and pitavastatin when 160 mg of micronized fenofibrate and 2 mg of pitavastatin are co-administered. The treatments were well tolerated during the study, with no serious adverse events.

[56] *Bandaru S, Ala C, Ekstrand M et al.* **Lack of RAC1 in macrophages protects against atherosclerosis**. PloS one 2020; 15:e0239284.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32941503
ABSTRACT
The Rho GTPase RAC1 is an important regulator of cytoskeletal dynamics, but the role of macrophage-specific RAC1 has not been explored during atherogenesis. We analyzed RAC1 expression in human carotid atherosclerotic plaques using immunofluorescence and found higher macrophage RAC1 expression in advanced plaques compared with intermediate human atherosclerotic plaques. We then produced mice with Rac1-deficient macrophages by breeding conditional floxed Rac1 mice (Rac1fl/fl) with mice expressing Cre from the macrophage-specific lysosome M promoter (LC). Atherosclerosis was studied in vivo by infecting Rac1fl/fl and Rac1fl/fl/LC mice with AdPCSK9 (adenoviral vector overexpressing proprotein convertase subtilisin/kexin type 9). Rac1fl/fl/LC macrophages secreted lower levels of IL-6 and TNF-α and exhibited reduced foam cell formation and lipid uptake. The deficiency of Rac1 in macrophages reduced the size of aortic atherosclerotic plaques in AdPCSK9-infected Rac1fl/fl/LC mice. Compare with controls, intima/media ratios, the size of necrotic cores, and numbers of CD68-positive macrophages in atherosclerotic plaques were reduced in Rac1-deficient mice. Moreover, we found that RAC1 interacts with actin-binding filamin A. Macrophages expressed increased RAC1 levels in advanced human atherosclerosis. Genetic

inactivation of RAC1 impaired macrophage function and reduced atherosclerosis in mice, suggesting that drugs targeting RAC1 may be useful in the treatment of atherosclerosis.

[57] *Floyd C, Crook M*. **Adverse events to PCSK-9 inhibitors: what is the current evidence?** Postgraduate medical journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32934180
ABSTRACT

[58] *Rodrigues WDR, Sarni ROS, Abad TTO et al.* **Lipid profile of pediatric patients with chronic rheumatic diseases - a retrospective analysis**. Rev Assoc Med Bras (1992) 2020; 66:1093-1099.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32935804
ABSTRACT
AIM: To describe the prevalence of dyslipidemia in children and adolescents with autoimmune rheumatic diseases (ARDs), particularly juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), and juvenile dermatomyositis (JDM). METHODS: Retrospective cross-sectional study conducted in the pediatric rheumatology outpatient clinic. We evaluated 186 children and adolescents between the ages of 5 and 19 years. The medical records were reviewed for the following data: demographic and clinical features, disease activity, and lipid profile (triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) and very low density lipoprotein (VLDL-C)). In addition, non-HDL cholesterol was calculated as TC minus HDL-C. The cut-off points proposed by the American Academy of Pediatrics were used to classify the lipid profile. RESULTS: Dyslipidemia was observed in 128 patients (68.8%), the most common being decreased HDL-C (74 patients, 39.8%). In the JIA group there was an association between the systemic subtype and altered LDL-C and NHDL-C, which demonstrated a more atherogenic profile in this subtype (p=0.027 and p=0.017, respectively). Among patients with jSLE, the cumulative corticosteroid dose was associated with an increase in LDL-C (p=0.013) and with a decrease in HDL-C (p=0.022). CONCLUSION: Dyslipidemia is common in children and adolescents with ARDs, especially JIA, jSLE, and JDM, and the main alteration in the lipid profile of these patients was decreased HDL-C.

[59] *Kong Y, Feng W, Zhao X et al.* **Statins ameliorate cholesterol-induced inflammation and improve AQP2 expression by inhibiting NLRP3 activation in the kidney**. Theranostics 2020; 10:10415-10433.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32929357
ABSTRACT
Background: Chronic kidney diseases (CKD) are usually associated with dyslipidemia. Statin therapy has been primarily recommended for the prevention of cardiovascular risk in patients with CKD; however, the effects of statins on kidney disease progression remain controversial. This study aims to investigate the effects of statin treatment on renal handling of water in patients and in animals on a high-fat diet. Methods: Retrospective cohort patient data were reviewed and the protein expression levels of aquaporin-2 (AQP2) and NLRP3 inflammasome adaptor ASC were examined in kidney biopsy specimens. The effects of statins on AQP2 and NLRP3 inflammasome components were examined in nlrp3(-/-) mice, 5/6 nephroectomized (5/6Nx) rats with a high-fat diet (HFD), and in vitro. Results: In the retrospective cohort study,

serum cholesterol was negatively correlated to eGFR and AQP2 protein expression in the kidney biopsy specimens. Statins exhibited no effect on eGFR but abolished the negative correlation between cholesterol and AQP2 expression. Whilst nlrp3(+/+) mice showed an increased urine output and a decreased expression of AQP2 protein after a HFD, which was moderately attenuated in nlrp3 deletion mice with HFD. In 5/6Nx rats on a HFD, atorvastatin markedly decreased the urine output and upregulated the protein expression of AQP2. Cholesterol stimulated the protein expression of NLRP3 inflammasome components ASC, caspase-1 and IL-1β, and decreased AQP2 protein abundance in vitro, which was markedly prevented by statins, likely through the enhancement of ASC speck degradation via autophagy. Conclusion: Serum cholesterol level has a negative correlation with AQP2 protein expression in the kidney biopsy specimens of patients. Statins can ameliorate cholesterol-induced inflammation by promoting the degradation of ASC speck, and improve the expression of aquaporin in the kidneys of animals on a HFD.

[60] *Král T*. **Praluent (alirokumab)**. Vnitr Lek 2020; 66:96-100.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32942879

ABSTRACT

PCSK9 inhibitors (inhibitors of proprotein convertase subtilisin/kexin type 9) offer a promising treatment strategy decreasing the concentrations of both atherogenic low density lipoprotein (LDL) and cholesterol contained within LDL. Alirocumab is one of two PCSK9 inhibitors that entered clinical practice so far. Alirocumab is a specific antibody against PCSK9, manufactured using recombinant technique. When the antibody binds to the PCSK9 isoenzyme, no complex encompassing PCSK9 and LDL receptor can be formed, thus enabling further recirculation of the LDL receptor. Increasing the amount of LDL receptors available on the cell membranes leads to higher internalization of LDL within cells and to lowering of LDL cholesterol concentration. It has been shown that alirocumab exerts favorable effect on atherogenic lipoproteins (i.e. decrease of concentrations of LDL cholesterol by more than 50%) both in monotherapy and in combination with statins or other hypolipidemics. Odyssey Outcomes study brought new information into light and changed the guidelines of treating the patients with cardivascular diseases. Alirokumab added to intensive statin therapy reduced significantly the risk of cardiovascular diseases and the post hoc analysis confirmed also the reduction of total death rate. The positive effect of alirocumab is higher in patients with higher initial LDL-C. The therapy with alirokumab is safe, with minimum adverse events.