[1] *Shapiro MD, Fazio S*. **Preventive cardiology as a dedicated clinical service: The past, the present, and the (Magnificent) future**. Am J Prev Cardiol 2020; 1:100011.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32835348
ABSTRACT
•Ischemic cardiovascular disease continues to be most common cause of death after age 55 everywhere in the world.•As the average person is exposed over life to a variety of artery-damaging insults it is easy to predict that this trend will continue for decades.•We face an unprecedented opportunity to consolidate, strengthen, and broaden the effort to prevent cardiovascular events, both ischemic and non ischemic.•This effort requires professional lifestyle counseling, dietary interventions, use of natural supplements, pharmacotherapy, and efficient cross-referral strategies.•The nascent subspecialty of preventive cardiology must reach uniformity in protocols of care, and must develop a system of training and certification for the next generation of expert providers.

[2] *Williams DM, Bandres-Ciga S, Heilbron K et al.* **Evaluating Lipid-Lowering Drug Targets for Parkinson's Disease Prevention with Mendelian Randomization**. Annals of neurology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32841444
ABSTRACT
Long-term exposure to lipid-lowering drugs might affect Parkinson's disease (PD) risk. We conducted Mendelian randomization analyses where genetic variants indexed expected effects of modulating lipid-lowering drug targets on PD. Statin exposure was not predicted to increase PD risk, although results were not precise enough to support benefits for prevention clearly (odds ratio [OR] = 0.83; 95% confidence interval [CI] = 0.65, 1.07). Other target results were null, except for variants indicating Apolipoprotein-A5 or Apolipoprotein-C3 inhibition might confer protection. These findings suggest peripheral lipid variation may not have a prominent role in PD etiology, but some related drug targets could influence PD via alternate pathways. ANN NEUROL 2020.

[3] *Ben-Aicha S, Casaní L, Muñoz-García N et al.* **HDL (High-Density Lipoprotein) Remodeling and Magnetic Resonance Imaging-Assessed Atherosclerotic Plaque Burden: Study in a Preclinical Experimental Model**. Arteriosclerosis, thrombosis, and vascular biology 2020; 40:2481-2493.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32847390
ABSTRACT
OBJECTIVE: HDL (high-density lipoprotein) role in atherosclerosis is controversial. Clinical trials with CETP (cholesterylester transfer protein)-inhibitors have not provided benefit. We have shown that HDL remodeling in hypercholesterolemia reduces HDL cardioprotective potential. We aimed to assess whether hypercholesterolemia affects HDL-induced atherosclerotic plaque regression. Approach and Results: Atherosclerosis was induced in New Zealand White rabbits for 3-months by combining a high-fat-diet and double-balloon aortic denudation. Then, animals underwent magnetic resonance imaging (basal plaque) and randomized to receive 4 IV infusions (1 infusion/wk) of HDL isolated from normocholesterolemic (NC-HDL; 75 mg/kg; n=10), hypercholesterolemic (HC-HDL; 75 mg/Kg; n=10), or vehicle (n=10) rabbits. Then, animals underwent a second magnetic resonance imaging (end plaque). Blood, aorta, and liver samples were obtained for analyses. Follow-up

magnetic resonance imaging revealed that NC-HDL administration regressed atherosclerotic lesions by 4.3%, whereas, conversely, the administration of HC-HDLs induced a further 6.5% progression (P<0.05 versus basal). Plaque characterization showed that HC-HDL administered animals had a 2-fold higher lipid and cholesterol content versus those infused NC-HDL and vehicle (P<0.05). No differences were observed among groups in CD31 levels, nor in infiltrated macrophages or smooth muscle cells. Plaques from HC-HDL administered animals exhibited higher Casp3 (caspase 3) content (P<0.05 versus vehicle and NC-HDL) whereas plaques from NC-HDL infused animals showed lower expression of Casp3, Cox1 (cyclooxygenase 1), inducible nitric oxide synthase, and MMP (metalloproteinase) activity (P<0.05 versus HC-HDL and vehicle). HDLs isolated from animals administered HC-HDL displayed lower antioxidant potential and cholesterol efflux capacity as compared with HDLs isolated from NC-HDL-infused animal and vehicle or donor HDL (P<0.05). There were no differences in HDL-ApoA1 content, ABCA1 (ATP-binding cassette transporter A1) vascular expression, and SRB1 (scavenger receptor B1) and ABCA1 liver expression. CONCLUSIONS: HDL particles isolated from a hypercholesterolemic milieu lose their ability to regress and stabilize atherosclerotic lesions. Our data suggest that HDL remodeling in patients with co-morbidities may lead to the loss of HDL atheroprotective functions.

[4] *Rallidis LS, Liberopoulos EN, Vlachopoulos C et al.* **Very high-risk familial hypercholesterolaemia patients in real life: The remaining gap in achieving the current LDL-C targets despite the use of PCSK9 inhibitors**. Atherosclerosis 2020; 309:67-69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32859385
ABSTRACT

[5] *Calder PC*. **Eicosapentaenoic and docosahexaenoic acid derived specialised pro-resolving mediators: Concentrations in humans and the effects of age, sex, disease and increased omega-3 fatty acid intake**. Biochimie 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32860894
ABSTRACT
Although inflammation has a physiological role, unrestrained inflammation can be detrimental, causing tissue damage and disease. Under normal circumstances inflammation is self-limiting with induction of active resolution processes. Central to these is the generation of specialised pro-resolving lipid mediators (SPMs) from eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These include resolvins, protectins and maresins whose activities have been well described in cell and animal models. A number of SPMs have been reported in plasma or serum in infants, children, healthy adults and individuals with various diseases, as well as in human sputum, saliva, tears, breast milk, urine, synovial fluid and cerebrospinal fluid and in human adipose tissue, skeletal muscle, hippocampus, skin, placenta, lymphoid tissues and atherosclerotic plaques. Differences in SPM concentrations have been reported between health and disease, as would be expected. However, sometimes SPM concentrations are lower in disease and sometimes they are higher. Human studies report that plasma or serum concentrations of some SPMs can be increased by increasing intake of EPA and DHA. However, the relationship of specific intakes of EPA and DHA to enhancement in the appearance of specific SPMs is not clear and needs a more thorough investigation. This is important because of the potential for EPA and DHA to be used more effectively in prevention and treatment of inflammatory conditions. If generation of SPMs represents an important

mechanism of action of EPA and DHA, then more needs to be known about the most effective strategies by which EPA and DHA can increase SPM concentrations.

[6] *Zheng L, Cai Y, Qiu B et al.* **Rosuvastatin Improves Cognitive Function of Chronic Hypertensive Rats by Attenuating White Matter Lesions and Beta-Amyloid Deposits**. BioMed research international 2020; 2020:4864017.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32851076
ABSTRACT
Hypertensive white matter lesion (WML) is one of common causes of vascular cognitive impairment. In this study, we aimed to investigate the effect of rosuvastatin on cognitive impairment and its underlying mechanisms in chronic hypertensive rats. From the 8(th) week after establishment of stroke-prone renovascular hypertensive rats (RHRSPs), rosuvastatin (10 mg/kg) or saline as a control was administrated once daily for consecutive 12 weeks by gastric gavage. Cognitive function was assessed with the Morris water maze test and novel object recognition test. WML was observed by Luxol fast blue staining. Aβ deposits, Claudin-5, Occludin, and ZO-1 were determined by immunofluorescence. After rosuvastatin treatment, the escape latencies were decreased and the time of crossing the hidden platform was increased in the Morris water maze, compared with the vehicle-treated RHRSP group. In a novel object recognition test, the recognition index in the rosuvastatin-treated RHRSP group was significantly larger than that in the vehicle-treated RHRSP group. Rosuvastatin treatment presented with the effects of lower WML grades, higher expression of tight junction proteins Claudin-5, Occludin, and ZO-1 in the corpus callosum, and less Aβ deposits in the cortex and hippocampus. The data suggested that rosuvastatin improved the cognitive function of chronic hypertensive rats partly by attenuating WML and reducing Aβ burden.

[7] *Liu SH, Yu J, Creeden JF et al.* **Repurposing metformin, simvastatin and digoxin as a combination for targeted therapy for pancreatic ductal adenocarcinoma**. Cancer letters 2020; 491:97-107.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32829010
ABSTRACT
Patients with pancreatic adenocarcinoma (PDAC) have a 5-year survival rate of 8%, the lowest of any cancer in the United States. Traditional chemotherapeutic regimens, such as gemcitabine- and fluorouracil-based regimens, often only prolong survival by months. Effective precision targeted therapy is therefore urgently needed to substantially improve survival. In an effort to expedite approval and delivery of targeted therapy to patients, we utilized a platform to develop a novel combination of FDA approved drugs that would target pancreaticoduodenal homeobox1 (PDX1) and baculoviral inhibitor of apoptosis repeat-containing 5 (BIRC5) utilizing super-promoters of the target genes to interrogate an FDA approved drug library. We identified and selected metformin, simvastatin and digoxin (C3) as a novel combination of FDA approved drugs, which were shown to effectively target PDX1 and BIRC5 in human PDAC tumors in mice with no toxicity.

[8] *Gomez-Barrado JJ, Gomez-Turegano P, Ortiz-Cortes C et al.* **Low-Density Lipoprotein Cholesterol Targets in Patients With Coronary Heart Disease in Extremadura (Spain): LYNX Registry**. Cardiology research 2020; 11:311-318.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849966

ABSTRACT
BACKGROUND: Low-density lipoprotein cholesterol (LDL-C) contributes decisively to the development of cardiovascular disease (CVD). In the LYNX registry we determined the rate of achievement of the target value of LDL-C, the use of lipid-lowering therapy (LLT) and the predictive factors of not reaching the target in patients with stable coronary heart disease (CHD). METHODS: LYNX included consecutive patients with stable CHD treated at the University Hospital of Caceres, Extremadura (Spain) from September 2016 to September 2018, and those who must have an LDL-C target below 70 mg/dL according to the European Society of Cardiology (ESC) 2016 guidelines. The variables independently associated with the breach of the LDL-C objective were evaluated by multivariable logistic regression. RESULTS: A total of 674 patients with stable CHD were included. The average LDL-C levels were 68.3 ± 24.5 mg/dL, with 56.7% showing a level below 70 mg/dL. LLT was used by 96.7% of patients, 71.7% were treated with high-powered statins and 30.1% with ezetimibe. The risk of not reaching the target value of LDL-C was higher in women, in active smokers, and in those who had multivessel CHD or had atrial fibrillation. Patients with diabetes mellitus, those who took potent statins or co-administration treatment with ezetimibe were more likely to reach the target level of LDL-C. CONCLUSIONS: The treatment of dyslipidemia in patients with chronic CHD remains suboptimal; however, an increasing number of very high-risk patients achieve the LDL-C objective, although there is still enormous potential to improve cardiovascular outcome through the use of more intensive LLT.

[9] *Yu Q, Ma X, Wang Y et al.* **Dietary Cholesterol Exacerbates Statin-Induced Hepatic Toxicity in Syrian Golden Hamsters and in Patients in an Observational Cohort Study**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32860619

ABSTRACT
PURPOSE: Statins are inhibitors of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase, which is involved in cholesterol synthesis. The major side effects of statins include muscle- and liver-related toxicity. Muscle toxicity is highly associated with polymorphisms in cytochrome P450 proteins (CYPs), as predicted by pharmacogenomics. However, the mechanisms of hepatotoxicity are not well understood. Due to differences in cholesterol metabolism, statins are well tolerated in mice. In contrast, hamsters exhibit metabolic traits similar to humans and are suitable for studying the hepatotoxicity of statins. METHODS: We investigated the effect of rosuvastatin (RSV) on liver damage in wild-type (WT) hamsters fed a high-cholesterol diet (HCD) and LDLR knockout (LDLR(-/-)) hamsters that developed spontaneous hypercholesterolemia. Two cohorts of clinical subjects (clinical registry number: 2017001) taking atorvastatin (ATV) were recruited for direct (assessment of cholesterol intake individually, n = 44) and indirect (celebratory meals/holiday season, n = 1993) examination of dietary cholesterol intake and liver damage, as indicated by elevation of alanine aminotransferase (ALT). RESULTS: RSV at a dose of 10 mg/kg caused fatal liver damage only in HCD-fed WT hamsters, while LDLR(-/-) hamsters with the same cholesterol levels were resistant to this toxic effect. In the human studies, we observed that the incidence of hepatic toxicity in patients receiving long-term ATV treatment was higher in patients with greater dietary cholesterol intake and in patients who consumed more food during Chinese holidays. CONCLUSION: Our results propose, for the first time, that dietary cholesterol significantly

contributes to statin-related hepatotoxicity, providing valuable insight into the clinical use of statins.

[10] *Aranzulla TC, Musumeci G*. **Morphological stabilization and regression of carotid plaque following therapy with evolocumab in a high-risk patient**. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32845075
ABSTRACT
Lipid-lowering therapy is a mainstay for the management of coronary and carotid disease. Actually, progression of atherosclerosis and adverse events are reduced in proportion to the achieved levels of LDL cholesterol (LDL-C). A 67-year-old patient underwent two hospitalizations 6 months apart due to acute coronary syndromes. In the first, PCI with drug-eluting stents (DES) was performed to treat ulcerated stenoses in the left anterior descending artery. In the second, lipid-rich critical disease was found on the right coronary artery and treated with PCI + DES. Later, carotid duplex ultra-sonography (DU) was done due to some episodes of dizziness. It showed an 80% critical stenosis (peak systolic velocity, PSV 239 cm/s) of the left internal carotid artery (LICA) with high-risk features (hypoechogenic and irregular plaque with "fluffy" components). In consideration of the plaque morphology and the unmet LDL-C targets, evolocumab was added to the ongoing statin therapy. In the following months, we observed a parallel trend between carotid plaque regression and LDL-C lowering. Initial plaque remodeling was seen after 5 months: the atheroma appeared fibrotic, with no more fluffy components. At 10 months, in conjunction with the achievement of LDL-C goal (23 mg/dl), a fibrocalcific atheroma was observed; PSV, after an initial rise, fell to 229 cm/s. No further cardiovascular event occurred at 46 months. Last DUS showed a 60% fibrocalcific mid LICA stenosis with PSV of 180 cm/s. Our experience highlights the important role of proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors in promoting remodeling and hopefully regression of atherosclerotic plaques.

[11] *Chang CC, Chang CY, Lin PC et al.* **Administration of low-dose resveratrol attenuated hepatic inflammation and lipid accumulation in high cholesterol-fructose diet-induced rat model of nonalcoholic fatty liver disease**. Chin J Physiol 2020; 63:149-155.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32859881
ABSTRACT
Resveratrol (RSV) has been demonstrated to ameliorate nonalcoholic fatty liver disease (NAFLD) in animal studies. However, RSV was given with the dosage that ranged from 7 to 300 mg/kg body weight (BW). Hence, the study aimed to investigate the efficacy of RSV at a lower dosage on high cholesterol-fructose diet (HCFD)-induced rat model of NAFLD. In the study, male Sprague-Dawley rats were fed with HCFD for 15 weeks. RSV was also given at a daily dose of 1 mg/kg BW for 15 days or 15 weeks by oral delivery. At sacrifice, plasma and liver specimens were acquired for detections of alanine and aspartate aminotransferases, proinflammatory cytokines, and lipid contents. Histological examinations and Western blotting analysis were performed using liver tissues. The results showed that RSV administration reduced plasma levels of aminotransferases and proinflammatory cytokines including interleukin-1 beta (IL-1β), IL-6, and tumor necrosis factor-alpha (TNF-α) in HCFD-induced NAFLD. RSV also mitigated hepatic lipid accumulation and expression of IL-1β, IL-6, and TNF-

α. Besides, phosphorylation of signal transducer and activator of transcription 3 (STAT3) was reduced with RSV supplementation in the liver of HCFD-fed rats. We concluded that low-dose RSV supplementation attenuated hepatic inflammation and lipid accumulation in HCFD-induced NAFLD. The ameliorative effect of RSV on NAFLD could be associated with downregulation of phosphorylated STAT3.

[12] *Ideishi A, Suematsu Y, Tashiro K et al.* **Changes in serum levels of angiopoietin-like protein-8 and glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1 after ezetimibe therapy in patients with dyslipidemia**. Clinica chimica acta; international journal of clinical chemistry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32858055
ABSTRACT

[13] *Södergren A, Askling J, Bengtsson K et al.* **Characteristics and outcome of a first acute myocardial infarction in patients with ankylosing spondylitis**. Clinical rheumatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32845439
ABSTRACT
OBJECTIVES: To study clinical characteristics, mortality, and secondary prevention, after a first incident acute myocardial infarction (AMI) in patients with ankylosing spondylitis (AS) compared with the general population. METHODS: In total, 292 subjects with AS and a first AMI between Jan 2006 and Dec 2014 were identified using the Swedish national patient register. Each subject was matched with up to 5 general population comparators per AS-patient (n = 1276). Follow-up started at the date of admission for AMI and extended until death or 365 days of follow-up. Cox regression was used to assess mortality in two time intervals: days 0-30 and days 31-365. For a subgroup with available data, clinical presentation at admission, course, treatment for AMI, and secondary prevention were compared. RESULTS: During the 365-day follow-up, 56/292 (19%) AS patients and 184/1276 (14%) comparators died. There were no difference in mortality due to cardiovascular-related causes, although the overall mortality day 31-365 was increased among patients with AS compared with comparators (HR [95% CI] = 2.0 [1.3;3.0]). At admission, AS patients had a higher prevalence of cardiovascular comorbidities compared with comparators. At discharge, patients with AS were less often prescribed lipid-lowering drugs and non-aspirin antiplatelet therapy. CONCLUSIONS: Patients with AS tend to have a higher comorbidity burden at admission for first AMI. The mortality after a first AMI due to cardiovascular-related causes does not seem to be elevated, despite an increased overall mortality during days 31-365 among patients with AS compared with the general population. Key Points • The all-cause mortality after a first AMI was higher in patients with AS. • Mortality after a first AMI due to CVD-related causes does not seem to be elevated for patients with AS. • In patients with AS suffering a first AMI, more attention should be given to other comorbidities causing an excess in mortality.

[14] *Ibrahim R, Salih M, Elmokdad C, Sidhu A*. **Diabetic Ketoacidosis, Very Severe Hypertriglyceridemia, and Pseudohyponatremia Successfully Managed With Insulin Infusion**. Cureus 2020; 12:e9306.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32832302
ABSTRACT

Hypertriglyceridemia is a common lipid abnormality that has serious consequences, such as acute pancreatitis and premature atherosclerosis. The consensus for first-line treatment to lower the triglyceride levels has not been fully evaluated. We present a case of very severe hypertriglyceridemia with diabetic ketoacidosis and an artifactual pseudohyponatremia. The patient was effectively and safely treated with guideline-directed medical therapy; however, it needed a longer duration of intravenous insulin. Therefore, our case has been in agreement with literature by concluding that insulin is in fact an effective and minimally invasive form to lower a high triglyceride level, especially in patients who have concurrent uncontrolled diabetes mellitus.

[15] *Malik J, Shabeer H, Ishaq U et al.* **Modern Lipid Management: A Literature Review**. Cureus 2020; 12:e9375.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32850243
ABSTRACT
Pro-protein convertase subtilisin/Kexin type 9 (PCSK9) inhibitors are relatively new, non-statin, lipid-lowering drugs that reduce low-density lipoprotein cholesterol (LDL-C) by 60%. PCSK9 inhibitors reduce the blood concentrations of cholesterol by the degradation of LDL receptors, which subsequently extracts cholesterol from cells. This leads to cardiovascular risk reduction in various at-risk populations, including atherosclerotic coronary artery disease. Despite their promise for advanced lipid-lowering ability, cost-effectiveness is a barrier to their routine use. While searching PubMed, we extracted land-mark trials on two of the anti-PCSK9 monoclonal antibodies, alirocumab and evolocumab. When combined with statins or ezetimibe, they show an exponential fall in LDL-C levels, helping achieve target values in high-risk populations and decreasing cardiovascular adverse events. Ongoing research is exploring the long-term efficacy of these antibodies in established coronary artery disease and familial hypercholesterolemia with more prospects for this novel lipid-lowering therapy.

[16] *Lagoutte-Renosi J, Flammang M, Chirouze C et al.* **Real-Life Impact on Lipid Profile of a Switch from Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in HIV-Infected Patients**. Curr HIV Res 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32838719
ABSTRACT
Tenofovir disoproxil fumarate is a prodrug of tenofovir diphosphate that exposes patients to renal toxicity over the long term. Tenofovir alafenamide, a new prodrug, now makes it possible to reduce toxicity, but at the cost of an alteration in lipid profile. There is currently no recommendation for follow-up of lipid profile when switching from tenofovir disoproxil fumarate to tenofovir alafenamide. <P> Objective: Our study aimed to evaluate the effects on renal function and lipid profile of a switch from tenofovir disoproxil fumarate to tenofovir alafenamide, and the consequences for patient management. <P> Methods: Demographic, clinical and biological data was recorded from a retrospective clinical cohort study in real-life, including patients who switched from tenofovir disoproxil fumarate to tenofovir alafenamide. A descriptive analysis of the study population, with comparison of biological parameters using the paired Student t test for paired data was performed. <P> Results: From January 2016 to January 2019, a total of 103 patients were included. There was no significant difference in renal function before vs after the switch in therapy (p=0.29 for creatinine, p=0.30 for phosphoremia). We observed a change in lipid profile, with a significant increase in total

cholesterol (p=0.0006), HDL cholesterol (p=0.0055) and triglycerides (p=0.0242). Four patients received lipid-lowering therapy after switching. <P> Conclusion: In patients who switch from tenofovir disoproxil fumarate to tenofovir alafenamide, lipid profile is altered, and may require initiation of lipid-lowering therapy. It seems necessary to monitor lipid parameters after this switch, despite the absence of an official recommendation.

[17] *Ramaswami U, Humphries SE*. **Management of familial hypercholesterolaemia in childhood**. Curr Opin Pediatr 2020; 32:633-640.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32833799
ABSTRACT
PURPOSE OF REVIEW: All guidelines for the management of heterozygous familial hypercholesterolaemia in children and young people recommend statins to lower LDL-cholesterol (LDL-C) concentrations, to reduce the individual's adult risk of developing cardiovascular disease (CVD). Here, we review recent findings regarding the efficacy and safety of the use of stains in childhood. RECENT FINDINGS: As expected from their safety profile in adults, there is no evidence from short-term trials or long-term follow-up that statin use in children is associated with any adverse effects on growth, pubertal development or muscle or liver toxicity. Long-term follow-up indicates benefits with respect to lower CVD rates. Factors that influence adherence are discussed, as is the role of the underlying genetic causes for hypercholesterolaemia and of variation at other genes in determining the LDL-C-lowering effect. SUMMARY: Based on the good safety profile, and the expert opinion guidelines, clinicians should consider prescribing statins for children with hypercholesterolaemia from the age of at least 10 years (and earlier if CVD risk is particularly high in the family). Uptitrating statin dosage and the use of additional lipid-lowering therapies should be considered so that LDL-C concentrations are lowered to recommended targets.

[18] *Mizus MC, Tiniakou E*. **Lipid-lowering Therapies in Myositis**. Curr Rheumatol Rep 2020; 22:70.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32845379
ABSTRACT
PURPOSE OF REVIEW: The use of lipid-lowering therapies in patients with idiopathic inflammatory myopathies (IIM) is complicated and there are no guidelines for diagnosing, monitoring, or treating atherosclerotic cardiovascular disease (ASCVD) in this group of patients. RECENT FINDINGS: The use of lipid-lowering therapies, especially statins, is recommended in patients with increased risk for ASCVD, which includes patients with inflammatory diseases, based on recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines for ASCVD management. There is accumulating evidence that patients with IIM are at increased risk for ASCVD, similar to other inflammatory diseases. Lipid-lowering therapies have side effects that may be pronounced or confounding in myositis patients, potentially limiting their use. Statins are specifically contraindicated in patients with anti 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) antibodies. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been shown to be safe and potentially beneficial in patients with IIM. Here, we propose a framework for (1) ASCVD risk assessment and treatment based on ACC/AHA ASCVD primary prevention guidelines; (2) myositis disease monitoring while undergoing lipid-lowering therapy; and (3) management of statin intolerance, including, indications for the use of PCSK9 inhibitors.

[19] *Sublette ME*. **Lipids and Suicide Risk**. Curr Top Behav Neurosci 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32840861
ABSTRACT
In the search for biomarkers and modifiable risk factors for suicide, lipid status has garnered considerable interest, although the lipid-suicide connection is not without controversy. Major categories of lipids that have been reported as germane to suicide include sterols and polyunsaturated fatty acids (PUFAs). Research concerning lipid effects on mood and suicide risk includes epidemiologic approaches, cohort studies, and clinical trials. In general, current evidence suggests that higher n-3 relative to n-6 PUFA intake may have beneficial effects on depression and suicide risk, particularly in women, while low cholesterol may be detrimental in both sexes. Additionally, low estrogen in women has been associated with suicide attempts, whereas high androgen loads may contribute to the higher suicide completion rate in men. Basic and translational research provides strong evidence for several potential mechanisms that have been implicated in depression and suicide. Firstly, PUFAs, cholesterol, and estrogen can interact to influence structure and function of membrane microdomains ("lipid rafts"), with potential regulatory effects on inflammation and signal transduction, including monoaminergic signaling. Secondly, PUFAs bind to and activate peroxisome proliferator-activated receptors (PPARs), nuclear receptors that regulate gene expression, with resultant effects on inflammation and bioenergetics. Thirdly, PUFAs are both a target for and a hormetic regulator of oxidative stress. Critical to a greater understanding of lipid status as a suicide risk predictor and treatment target will be studies that map genomic and phenotypic characteristics of individuals whose emotional state is affected most by lipid status. Also important will be a more nuanced understanding of lipid-lipid interactions and the differential roles of lipid subclasses on suicide risk.

[20] *Fan Y, Wang D, Rao C et al.* **Atorvastatin Combined with Low-Dose Dexamethasone Treatment Protects Endothelial Function Impaired by Chronic Subdural Hematoma via the Transcription Factor KLF-2**. Drug design, development and therapy 2020; 14:3291-3299.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32848367
ABSTRACT
OBJECTIVE: Our previous study showed that the combination therapy with atorvastatin and low-dose dexamethasone protected endothelial cell function in chronic subdural hematoma (CSDH) injury. In this study, we aimed to investigate the mechanism underlying the effects of this combination therapy on CSDH-induced cell dysfunction. METHODS: Monocytes and endothelial cells were cocultured with CSDH patient hematoma samples to mimic the pathological microenvironment of CSDH. Monocytes (THP-1 cells) and endothelial cells (hCMEC/D3 cells) were cocultured in a transwell system for 24 h before stimulation with hematoma samples diluted in endothelial cell medium (ECM) at a 1:1 ratio. Tight junction markers were detected by Western blotting, PCR and immunofluorescence. hCMEC/D3 cells were collected for Western blot and PCR analyses to detect changes in the expression levels of vascular cell adhesion molecule (VCAM-1), intercellular adhesion molecule (ICAM-1), and Kruppel-like factor 2 (KLF-2). The IL-6, IL-10 and VEGF levels in the supernatant were measured by enzyme-linked immunosorbent assay (ELISA). RESULTS: KLF-2 expression in endothelial cells was decreased after stimulation with CSDH patient hematoma samples, but combination therapy with atorvastatin and low-dose dexamethasone reversed this trend. KLF-2

protected injured cells by increasing the expression of VE-cadherin and ZO-1; attenuating the expression of VCAM-1, ICAM-1, IL-6 and VEGF; and enhancing the expression of IL-10, all of which play pivotal roles in endothelial inflammation. Moreover, the effect of combination therapy with atorvastatin and low-dose dexamethasone was obviously reduced in endothelial cells with KLF-2 knockdown compared with normal cells. CONCLUSION: Coculture with hematoma samples decreased KLF-2 expression in human cerebral endothelial cells. Combination therapy with atorvastatin and low-dose dexamethasone counteracted hematoma-induced KLF-2 suppression in human cerebral endothelial cells to attenuate robust endothelial inflammation and permeability. KLF-2 plays an important role in drug therapy for CSDH and may become the key factor in treatment and prognosis.

[21] *Schooling CM, Zhao JV, Au Yeung SL, Leung GM*. **Investigating pleiotropic effects of statins on ischemic heart disease in the UK Biobank using Mendelian randomisation**. eLife 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32838838
ABSTRACT
We examined whether specifically statins, of the major lipid modifiers (statins, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and ezetimibe) have pleiotropic effects on ischemic heart disease (IHD) via testosterone in men or women. As a validation, we similarly assessed whether a drug that unexpectedly likely increases IHD also operates via testosterone. Using previously published genetic instruments we conducted a sex-specific univariable and multivariable Mendelian randomization study in the UK Biobank, including 179918 men with 25410 IHD cases and 212080 women with 12511 IHD cases. Of these three lipid modifiers, only genetically mimicking the effects of statins in men affected testosterone, which partly mediated effects on IHD. Correspondingly, genetically mimicking effects of anakinra on testosterone and IHD presented a reverse pattern to that for statins. These insights may facilitate the development of new interventions for cardiovascular diseases as well as highlighting the importance of sex-specific explanations, investigations, prevention and treatment.

[22] *Wang M, Hou ZH, Xu H et al.* **Ambient air pollution, traffic proximity and coronary atherosclerotic phenotype in China**. Environ Res 2020; 188:109841.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32846635
ABSTRACT
BACKGROUND: Exposure to ambient air pollution is associated with cardiovascular risk, potentially via atherosclerosis promotion. The disease mechanisms underlying these associations remain uncertain. OBJECTIVES: We aim to investigate the relationship of air pollution and traffic proximity with subclinical atherosclerosis, using coronary plaque phenotypes to gain insight into potential mechanisms. METHODS: Coronary plaque total and component volumes, high-risk plaque (HRP) appearance, and luminal stenosis were characterized by coronary computed tomography angiography in 2279 patients with atherosclerosis at baseline between 2014 and 2017. Annual average exposure to air pollutants including fine particulate matter (PM(2.5)), nitrogen dioxide (NO(2)), and ozone (O(3)) was estimated by air pollution models for individual participants. Multiple linear regression models were used to assess the association of each exposure with plaque phenotypes and coronary stenosis, controlling for potential confounders. Multiple logistic regression models were used to

estimate associations with plaque vulnerability. RESULTS: The studied population was 60.2±9.2 years old. PM(2.5) and NO(2) concentrations were significantly associated with a 5.0% (95%CI: 0.3, 9.9%, per 15 μg/m(3) increase for PM(2.5)), 12.0% (95%CI: 2.5, 22.5% per 20 μg/m(3) for NO(2)) larger volume of non-calcified plaque, respectively. Increase in O(3) concentration was associated with a 12.2% (95%CI: 2.2, 23.2%, per 5 μg/m(3) O(3)) larger volume of calcified plaque and a 12.8% (95%CI: 0.9, 26.2%) greater lumen narrowing. Increased PM(2.5) and NO(2), was also associated with increase in HRP, determined by the napkin ring sign (odds ratio: 1.41 [95%CI: 1.10, 1.80] for PM(2.5) and 1.78 [95%CI: 1.20, 2.63] for NO(2)) and positive remodeling index (OR: 1.11 [95%CI: 1.01, 1.21] for PM(2.5) and 1.20 [95%CI: 1.02, 1.42] for NO(2)), respectively, indicating increased plaque vulnerability. CONCLUSION: Long-term exposures to air pollution were associated with greater plaque volume and luminal stenosis, and increased plaque vulnerability with attendant risk of plaque rupture and erosion.

[23] *Gaudet D, Karwatowska-Prokopczuk E, Baum SJ et al.* **Vupanorsen, an N-acetyl galactosamine-conjugated antisense drug to ANGPTL3 mRNA, lowers triglycerides and atherogenic lipoproteins in patients with diabetes, hepatic steatosis, and hypertriglyceridaemia**. European heart journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32860031
ABSTRACT
AIMS : Loss-of-function mutations in ANGPTL3 are associated with beneficial effects on lipid and glucose metabolism and reduced risk of coronary artery disease. Vupanorsen (AKCEA-ANGPTL3-L Rx) is an N-acetyl galactosamine-conjugated antisense oligonucleotide targeted to the liver that selectively inhibits angiopoietin-like 3 (ANGPTL3) protein synthesis. METHODS AND RESULTS : This was a double-blind, placebo-controlled, dose-ranging, Phase 2 study. Patients (N =105) with fasting triglycerides >150 mg/dL (>1.7 mmol/L), type 2 diabetes, and hepatic steatosis were treated for 6 months with 40 or 80 mg every 4 weeks (Q4W), or 20 mg every week (QW) of vupanorsen, or placebo given subcutaneously. The primary efficacy endpoint was per cent change in fasting triglycerides from baseline at 6 months. Median baseline triglycerides were 2.84 mmol/L (252 mg/dL). Significant reductions in triglycerides of 36%, 53%, 47%, and in ANGPTL3 of 41%, 59%, 56%, were observed in the 40 mg Q4W, 80 mg Q4W, and 20 mg QW groups, respectively, compared with 16% reduction in triglycerides and 8% increase in ANGPTL3 in placebo. Compared with placebo, vupanorsen 80 mg Q4W reduced apolipoprotein C-III (58%), remnant cholesterol (38%), total cholesterol (19%), non-high-density lipoprotein cholesterol (HDL-C; 18%), HDL-C (24%), and apolipoprotein B (9%). There was no improvement in glycaemic parameters, or hepatic fat fraction. Treatment with vupanorsen was not associated with clinically significant changes in platelet counts, and the most common adverse events were those at the injection site, which were generally mild. CONCLUSION : Vupanorsen results in a favourable lipid/lipoprotein profile and provides a potential strategy for residual cardiovascular risk reduction.

[24] *Navarrete-Muñoz EM, Vioque J, Toledo E et al.* **Dietary folate intake and metabolic syndrome in participants of PREDIMED-Plus study: a cross-sectional study**. European journal of nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32833162
ABSTRACT

PURPOSE: We examined the association between dietary folate intake and a score of MetS (metabolic syndrome) and its components among older adults at higher cardiometabolic risk participating in the PREDIMED-Plus trial. METHODS: A cross-sectional analysis with 6633 with overweight/obesity participants with MetS was conducted. Folate intake (per 100 mcg/day and in quintiles) was estimated using a validated food frequency questionnaire. We calculated a MetS score using the standardized values as shown in the formula: [(body mass index + waist-to-height ratio)/2] + [(systolic blood pressure + diastolic blood pressure)/2] + plasma fasting glucose-HDL cholesterol + plasma triglycerides. The MetS score as continuous variable and its seven components were the outcome variables. Multiple robust linear regression using MM-type estimator was performed to evaluate the association adjusting for potential confounders. RESULTS: We observed that an increase in energy-adjusted folate intake was associated with a reduction of MetS score (β for 100 mcg/day = - 0.12; 95% CI: - 0.19 to - 0.05), and plasma fasting glucose (β = - 0.03; 95% CI: - 0.05 to - 0.02) independently of the adherence to Mediterranean diet and other potential confounders. We also found a positive association with HDL-cholesterol (β = 0.07; 95% CI: 0.04-0.10). These associations were also observed when quintiles of energy-adjusted folate intake were used instead. CONCLUSION: This study suggests that a higher folate intake may be associated with a lower MetS score in older adults, a lower plasma fasting glucose, and a greater HDL cholesterol in high-risk cardio-metabolic subjects.

[25] *Akasaka T, Kubo T*. **OCT-derived coronary calcified nodules as a predictor of high-risk patients**. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2020; 16:361-363.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32855116
ABSTRACT

[26] *Johnson TW, Joshi N*. **Vulnerable plaque imaging - a clinical reality?** EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2020; 16:364-366.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32855117
ABSTRACT

[27] *Borén J, Packard CJ, Taskinen MR*. **The Roles of ApoC-III on the Metabolism of Triglyceride-Rich Lipoproteins in Humans**. Frontiers in endocrinology 2020; 11:474.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849270
ABSTRACT
Cardiovascular disease (CVD) is the leading cause of death globally. It is well-established based on evidence accrued during the last three decades that high plasma concentrations of cholesterol-rich atherogenic lipoproteins are causatively linked to CVD, and that lowering these reduces atherosclerotic cardiovascular events in humans (1-9). Historically, most attention has been on low-density lipoproteins (LDL) since these are the most abundant atherogenic lipoproteins in the circulation, and thus the main carrier of cholesterol into the artery wall. However, with the rise of obesity and insulin resistance in many populations, there is increasing interest in the role of triglyceride-rich lipoproteins (TRLs) and their metabolic remnants, with accumulating evidence showing they too are causatively linked to CVD. Plasma triglyceride, measured either in the fasting or non-fasting state, is a useful index of the

abundance of TRLs and recent research into the biology and genetics of triglyceride heritability has provided new insight into the causal relationship of TRLs with CVD. Of the genetic factors known to influence plasma triglyceride levels variation in APOC3- the gene for apolipoprotein (apo) C-III - has emerged as being particularly important as a regulator of triglyceride transport and a novel therapeutic target to reduce dyslipidaemia and CVD risk (10).

[28] *Sun L, Zhang W, Zhao Y et al.* **Dendritic Cells and T Cells, Partners in Atherogenesis and the Translating Road Ahead**. Frontiers in immunology 2020; 11:1456.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849502

ABSTRACT

Atherosclerosis is a chronic process associated with arterial inflammation, the accumulation of lipids, plaque formation in vessel walls, and thrombosis with late mortal complications such as myocardial infarction and ischemic stroke. Immune and inflammatory responses have significant effects on every phase of atherosclerosis. Increasing evidence has shown that both innate and adaptive "arms" of the immune system play important roles in regulating the progression of atherosclerosis. Accumulating evidence suggests that a unique type of innate immune cell, termed dendritic cells (DCs), play an important role as central instigators, whereas adaptive immune cells, called T lymphocytes, are crucial as active executors of the DC immunity in atherogenesis. These two important immune cell types work in pairs to establish pro-atherogenic or atheroprotective immune responses in vascular tissues. Therefore, understanding the role of DCs and T cells in atherosclerosis is extremely important. Here, in this review, we will present a complete overview, based on existing knowledge of these two cell types in the atherosclerotic microenvironment, and discuss some of the novel means of targeting DCs and T cells as therapeutic tactics for the treatment of atherosclerosis.

[29] *Hu Y, Wang X, Ye L et al.* **Rosuvastatin Alleviates Intestinal Injury by Down-Regulating the CD40 Pathway in the Intestines of Rats Following Traumatic Brain Injury**. Frontiers in neurology 2020; 11:816.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849246

ABSTRACT

Statins have been reported to suppress CD40 expression and nuclear factor (NF)-κB activation, which are both up-regulated in the intestines following traumatic brain injury (TBI)-induced intestinal injury. In this study, we aimed to investigate the effects of the statin rosuvastatin on post-TBI jejunal injury in rats, focusing on potential mechanisms involving the CD40/NF-κB signaling pathway. The jejunal CD40 expression was determined by western blotting. The DNA-binding activity of NF-κB was assessed by electrophoretic mobility shift assays (EMSAs). The tumor necrosis factor (TNF)-α and interleukin (IL)-1β levels were assessed by enzyme-linked immunosorbent assays (ELISAs). The severity of the jejunal mucosal injury was assessed by hematoxylin and eosin (HE) staining and histopathological evaluation. We found that the post-TBI upregulation of both CD40 expression and NF-κB activity in the jejunal tissues were significantly inhibited by rosuvastatin, while the post-TBI expression of TNF-α and IL-1β was significantly suppressed by rosuvastatin. In addition, rosuvastatin significantly ameliorated TBI-induced effects on the villus height, crypt depth, and villous surface area. Rosuvastatin suppressed TBI-induced intestinal injury in rats, which may be associated with the blockade of the CD40/NF-κB pathway.

[30] *Yang WJ, Abrigo J, Soo YO et al.* **Regression of Plaque Enhancement Within Symptomatic Middle Cerebral Artery Atherosclerosis: A High-Resolution MRI Study**. Frontiers in neurology 2020; 11:755.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849214

ABSTRACT

Objective: Contrast enhancement is a vital feature of the intracranial atherosclerotic plaque on high-resolution magnetic resonance imaging (HRMRI), but its clinical significance is still unclear. We aimed to quantitatively assess plaque enhancement patterns in the middle cerebral artery (MCA) atherosclerotic plaque. Methods: We conducted a cross-sectional study by prospectively recruiting stroke or transient ischemic attack patients with >30% of MCA stenosis of either side. All patients underwent contrast-enhanced HRMRI scans. Enrolled patients were classified into acute phase (<4 weeks), subacute phase (4-12 weeks) and chronic phase (>12 weeks) groups based on the time interval from stroke onset to imaging scan. Plaque enhancement index was calculated for each MCA lesion at the maximal narrowing site. Results: We identified a total of 89 MCA plaques [53 (60%) symptomatic and 36 (40%) asymptomatic; 57 (64%) acute, 18 (20%) subacute and 14 (16%) chronic] in 58 patients on HRMRI. Among the acute lesions, symptomatic plaques had a significantly stronger plaque enhancement than asymptomatic plaques (symptomatic vs. asymptomatic: 38.9 ± 18.2 vs. 18.2 ± 16.2, $p < 0.001$). Among the symptomatic lesions, plaque enhancement diminished with increasing time after stroke onset (38.9 ± 18.2, 22.0 ± 22.8, and 5.0 ± 10.1 for acute, subacute, and chronic phase, respectively; $p = 0.001$). Conclusion: Plaque enhancement in the acute atherosclerotic plaque is closely related to recent ischemic events. In symptomatic atherosclerosis, plaque enhancement regresses over time after ischemic stroke, which may offer the potential to monitor the plaque activity in intracranial atherosclerosis using HRMRI.

[31] *Zwickl H, Hackner K, Köfeler H et al.* **Reduced LDL-Cholesterol and Reduced Total Cholesterol as Potential Indicators of Early Cancer in Male Treatment-Naïve Cancer Patients With Pre-cachexia and Cachexia**. Frontiers in oncology 2020; 10:1262.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32850383

ABSTRACT

Cancer cachexia is characterized by the impairment of glucose and lipid homeostasis, the acceleration of processes promoting the mobilization of energy-rich compounds (e.g., insulin resistance, gluconeogenesis, and lipolysis) and the simultaneous activation of highly energy-demanding processes (e.g., systemic inflammation and activation of brown adipose tissue). We hypothesized that these processes might themselves change during cancer cachexia progression, such that plasma levels of glucose and lipids might be used to distinguish between the non-malignant state, pre-cachexia and cachexia. We performed an initial cross-sectional study including 60 treatment naïve cancer patients (38 with cancer cachexia and 22 with cancer pre-cachexia) and 61 patients without malignancy (21 with metabolic syndrome and 40 controls). Differences in lipids (total cholesterol, LDL and HDL cholesterol) and plasma fasting glucose were analyzed across various group configurations, with adjustments to age and antidiabetic or lipid-lowering drugs. Our study showed that levels of LDL cholesterol and total cholesterol might indicate cachexia stages irrespective of the presence of metabolic syndrome or lipid-lowering medication. High levels of plasma glucose were only seen in cachectic cancer patients on antidiabetics. These observations indicate that markers of

metabolic dysregulation associated with cachexia progression might be exploited for early detection of malignancy.

[32] *Gupta R, Ranchal P, Mahajan S et al.* **Lipid inclusions in cardiac myocytes - a rare case of cardiolipotoxicity**. Future cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32842772
ABSTRACT
The heart oxidizes fatty acids for its energy production. The physiological balance between fatty acid uptake and its oxidation prevents lipid accumulation in cardiac myocytes. However, accumulation of lipids due to various processes such as obesity, diabetes, heart failure, myocardial ischemia or infarction can result in damage to the heart tissue, also known as cardiolipotoxicity. We present a unique case of a 69-year-old gentleman with a history of heart failure and ventricular tachycardia. Endomyocardial biopsy to assess for restrictive cardiomyopathy/amyloid showed no evidence of amyloid, significant inflammation or fibrosis, but did show intracellular accumulation of significant amorphous material in most cardiac myocytes. We review the literature regarding the pathogenesis of cardiolipotoxicity, which has no definite cause or treatment yet identified.

[33] *Kho PF, Amant F, Annibali D et al.* **Mendelian randomization analyses suggest a role for cholesterol in the development of endometrial cancer**. International journal of cancer 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32851660
ABSTRACT
Blood lipids have been associated with the development of a range of cancers, including breast, lung and colorectal cancer. For endometrial cancer, observational studies have reported inconsistent associations between blood lipids and cancer risk. To reduce biases from unmeasured confounding, we performed a bidirectional, two-sample Mendelian randomization analysis to investigate the relationship between levels of three blood lipids (low-density lipoprotein [LDL] and high-density lipoprotein [HDL] cholesterol, and triglycerides) and endometrial cancer risk. Genetic variants associated with each of these blood lipid levels ($P < 5 \times 10(-8)$) were identified as instrumental variables, and assessed using genome-wide association study data from the Endometrial Cancer Association Consortium (12 906 cases and 108 979 controls) and the Global Lipids Genetic Consortium (n = 188 578). Mendelian randomization analyses found genetically raised LDL cholesterol levels to be associated with lower risks of endometrial cancer of all histologies combined, and of endometrioid and non-endometrioid subtypes. Conversely, higher genetically predicted HDL cholesterol levels were associated with increased risk of non-endometrioid endometrial cancer. After accounting for the potential confounding role of obesity (as measured by genetic variants associated with body mass index), the association between genetically predicted increased LDL cholesterol levels and lower endometrial cancer risk remained significant, especially for non-endometrioid endometrial cancer. There was no evidence to support a role for triglycerides in endometrial cancer development. Our study supports a role for LDL and HDL cholesterol in the development of non-endometrioid endometrial cancer. Further studies are required to understand the mechanisms underlying these findings.

[34] *Vázquez-Bourgon J, Mayoral-van Son J, Gómez-Revuelta M et al.* **Treatment discontinuation impact on long-term (10-years) weight gain and lipid metabolism in first-episode psychosis: results from the PAFIP-10 cohort**. The international journal of neuropsychopharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32840607
ABSTRACT
BACKGROUND: Patients with a first episode of psychosis (FEP) are at higher risk of gaining weight and presenting metabolic disturbances, partly related to antipsychotic exposure. Previous studies suggest that treatment discontinuation might have a positive impact on weight in schizophrenia. The aim of this study is to evaluate the effect of treatment discontinuation on weight and metabolic changes in a FEP cohort. METHODS: Two-hundred and nine FEP patients and 57 healthy controls were evaluated at study entry and prospectively at 10-years follow-up. Anthropometric measures, clinical, metabolic and sociodemographic data was collected. RESULTS: Patients discontinuing antipsychotic treatment presented a significant lower increase in weight and better metabolic parameters' results than those still on antipsychotic treatment at 10-years follow-up. CONCLUSIONS: Treatment discontinuation had a positive effect on the weight and metabolic changes observed in FEP patients; however, this effect was not sufficient for reaching the complete reversal to normal levels.

[35] *Altwairgi AK, Alghareeb WA, AlNajjar FH et al.* **Atorvastatin in combination with radiotherapy and temozolomide for glioblastoma: a prospective phase II study**. Invest New Drugs 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32851510
ABSTRACT
Glioblastoma is a fast-growing primary brain tumor observed in adults with the worst prognosis. Preclinical studies have demonstrated the encouraging anticancer activity of statins. This study evaluated the efficacy of atorvastatin in combination with standard therapy in patients with glioblastoma. In this prospective, open-label, single-arm, phase II study, patients were treated with atorvastatin in combination with the standard glioblastoma therapy comprising radiotherapy and temozolomide. The primary endpoint was progression-free survival (PFS) at 6 months (PFS-6). Among 36 patients enrolled from January 2014 to January 2017, the median age was 52 (20-69) years; 22% of the patients were aged ≥60 years, and 62% were male. Patients received atorvastatin for a median duration of 6.2 (0.3-28) months. At a median follow-up of 19 months, the PFS-6 rate was 66%, with a median PFS of 7.6 (5.7-9.4) months. In terms of Grade ≥ 3 hematological adverse events, thrombocytopenia and neutropenia occurred in 7% and 12% of patients, respectively. In multivariate analyses, high baseline low-density lipoprotein levels were associated with worse survival (P = 0.046). Atorvastatin was not shown to improve PFS-6. However, this study identified that high low-density lipoprotein levels are an independent predictor of poor cancer-related outcomes. Future clinical trials testing statins should aim to enroll patients with slow-growing tumors.Clinical trial information: NCT0202957 (December 12, 2013).

[36] *Cesaro A, Schiavo A, Moscarella E et al.* **Lipoprotein(a): a genetic marker for cardiovascular disease and target for emerging therapies**. Journal of cardiovascular medicine (Hagerstown, Md.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32858625

ABSTRACT
: Lipoprotein(a) [Lp(a)] is an established cardiovascular risk factor, and growing evidence indicates its causal association with atherosclerotic disease because of the proatherogenic low-density lipoprotein (LDL)-like properties and the prothrombotic plasminogen-like activity of apolipoprotein(a) [apo(a)]. As genetics significantly influences its plasma concentration, Lp(a) is considered an inherited risk factor of atherosclerotic cardiovascular disease (ASCVD), especially in young individuals. Moreover, it has been suggested that elevated Lp(a) may significantly contribute to residual cardiovascular risk in patients with coronary artery disease and optimal LDL-C levels. Nonetheless, the fascinating hypothesis that lowering Lp(a) could reduce the risk of cardiovascular events - in primary or secondary prevention - still needs to be demonstrated by randomized clinical trials. To date, no specific Lp(a)-lowering agent has been approved for reducing the lipoprotein levels, and current lipid-lowering drugs have limited effects. In the future, emerging therapies targeting Lp(a) may offer the possibility to further investigate the relation between Lp(a) levels and cardiovascular outcomes in randomized controlled trials, ultimately leading to a new era in cardiovascular prevention. In this review, we aim to provide an updated overview of current evidence on Lp(a) as well as currently investigated therapeutic strategies that specifically address the reduction of the lipoprotein.

[37] *Colivicchi F, Di Fusco SA, Scicchitano P et al.* **Updated clinical evidence and place in therapy of bempedoic acid for hypercholesterolemia: ANMCO position paper**. Journal of cardiovascular medicine (Hagerstown, Md.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32842050
ABSTRACT
: The central role of high low-density lipoprotein cholesterol levels in atherosclerotic cardiovascular disease has led to research focused on lipid-lowering agents for cardiovascular risk reduction. Bempedoic acid is an emerging treatment for hypercholesterolemia that has recently been approved for marketing in the United States and Europe. This review focuses on its mechanism of action and summarizes the main preclinical study findings. Furthermore, we report the clinical evidence supporting and guiding its use in hypercholesterolemia management.

[38] *Ohtani R, Nirengi S, Sakane N*. **Association Between Serum Apolipoprotein A1 Levels, Ischemic Stroke Subtypes and Plaque Properties of the Carotid Artery**. Journal of clinical medicine research 2020; 12:598-603.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849948
ABSTRACT
BACKGROUND: This study aimed to investigate the association between serum apolipoprotein A1 (ApoA1) levels, ischemic stroke subtypes and plaque properties. METHODS: We enrolled 92 patients with ischemic stroke and 21 age-matched controls (CONT). The stroke patients were divided into three subtypes: cardioembolic (CE, n = 15), atherothrombotic infraction (ATBI, n = 52), and lacunar infarction (LI, n = 25). Carotid plaques were classified as low, intermediate, or high intensity, and either simple or mixed type. Serum lipids (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG)), ApoA1, and ApoB were analyzed using commercially available kits. RESULTS: There was no difference in TC, LDL-C, HDL-C, and ApoB levels among the four groups. Serum ApoA1 levels in the ATBI group were significantly

lower compared with the CONT group. Among the ATBI group, the serum ApoA1 levels in the low-intensity plaque-type were significantly lower than those in the intermediate or hard-intensity plaque-type. Furthermore, serum ApoA1 levels in the mixed plaque-type were significantly lower than those in the simple type. CONCLUSIONS: These findings suggest that serum ApoA1 levels might be associated with the development of ATBI and plaque properties of the carotid artery.

[39] *Nath P, Panigrahi MK, Sahu MK et al.* **Effect of Exercise on NAFLD and Its Risk Factors: Comparison of Moderate versus Low Intensity Exercise**. Journal of clinical and translational hepatology 2020; 8:120-126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32832391
ABSTRACT
Background and Aims: Lifestyle (exercise and dietary) modification is the mainstay of treatment for non-alcoholic fatty liver disease (NAFLD). However, there is paucity of data on effect of intensity of exercise in management of NAFLD, and we aimed to study the effect of variable intensities of exercise on NAFLD. Methods: The study was performed in the Department of Gastroenterology of the SCB Medical College, Cuttack and the Biju Patnaik State Police Academy, Bhubaneswar. The subjects were police trainees [18 in a moderate intensity exercise group (MIG) and 19 in a low intensity exercise group (LIG)] recruited for a 6-month physical training course (261.8 Kcalorie, 3.6 metabolic equivalent in MIG and 153.6 Kcalorie, 2.1 metabolic equivalent in LIG). NAFLD was diagnosed by ultrasonography, with exclusion of all secondary causes of steatosis. All participants were evaluated by anthropometry (weight, height, body mass index (BMI), waist circumference), assessed for blood pressure and biochemical parameters (blood glucose, liver function test, lipid profile, serum insulin), and subjected to transabdominal ultrasonography before and after 6 months of physical training, and the results were compared. Results: Both the groups had similar BMI, fasting plasma glucose, AST, gamma-glutamyl transpeptidase, insulin, and homeostatic model assessment-insulin resistance (known as HOMA-IR) ($p>0.05$). However, subjects in the LIG were older and had lower alanine transaminase, higher triglycerides and lower high-density lipoproteins than MIG subjects. There was a significant reduction in BMI (27.0±2.1 to 26.8±2.0; $p=0.001$), fasting blood glucose (106.7±21.6 to 85.8±19.0; $p<0.001$), serum triglycerides (167.5±56.7 to 124.6±63.5; $p=0.017$), total cholesterol (216.8±29.2 to 196.7±26.6; $p=0.037$), low-density lipoprotein cholesterol (134.6±21.4 to 130.5±21.9; $p=0.010$), serum aspartate transaminase (39.3±32.2 to 30.9±11.4; $p<0.001$), serum alanine transaminase (56.6±28.7 to 33.0±11.3; $p<0.001$) and HOMA-IR (2.63±2.66 to 1.70±2.59; $p<0.001$) in the MIG. However, changes in these parameters in the LIG were non-significant. Hepatic steatosis regressed in 66.7% of the NAFLD subjects in the MIG but in only 26.3% of the LIG NAFLD subjects ($p=0.030$). Conclusions: Moderate rather than low intensity physical activity causes significant improvement in BMI, serum triglycerides, cholesterol, serum transaminases and HOMA-IR, and regression of ultrasonographic fatty change in liver among NAFLD subjects.

[40] *Khaire AA, Thakar SR, Wagh GN, Joshi SR*. **Placental lipid metabolism in preeclampsia**. Journal of hypertension 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32833919
ABSTRACT

OBJECTIVES: The current study examines the placental and maternal lipid profile and expression of genes involved in placental lipid metabolism in women with preeclampsia. METHODS: The current study includes normotensive control women (n=40) and women with preeclampsia (n=39). Preeclampsia women were further classified into women delivering at term preeclampsia (T-PE; n=15) and preterm preeclampsia (PT-PE; n=24). RESULTS: There were no significant differences in maternal lipid profile between the T-PE and normotensive control groups. Maternal plasma VLDL ($P<0.05$) and ratios of total cholesterol:HDL ($P<0.05$), atherogenic index [log (triglycerides/HDL)] ($P<0.01$) and apolipoprotein B:apolipoprotein A ($P<0.05$) were higher in the PT-PE group as compared with the normotensive control group. Placental total cholesterol and HDL levels were higher ($P<0.05$) in the T-PE as compared with the normotensive control group. Higher placental triglycerides ($P<0.05$) were observed in PT-PE group compared with T-PE group. Placental mRNA levels of peroxisome proliferator activated receptor α, carnitine palmitoyl transferase-1, cluster of differentiation 36 and lipoprotein lipases were lower ($P<0.05$) in the PT-PE than normotensive control group. A negative association of mRNA levels of peroxisome proliferator activated receptor α ($r=-0.246$, $P=0.032$; $r=-0.308$, $P=0.007$, respectively), carnitine palmitoyl transferase-1 ($r=-0.292$, $P=0.011$; $r=-0.366$, $P=0.001$), lipoprotein lipases ($r=-0.296$, $P=0.010$; $r=-0.254$, $P=0.028$) with SBP and DBP was observed. There was a positive association of placental triglycerides ($r=0.244$, $P=0.031$) with DBP. CONCLUSION: Women with preeclampsia exhibit higher lipid:lipoprotein ratios suggesting an atherogenic state particularly in women delivering preterm. Lower expression of genes involved in placental fatty acid oxidation and transport was also observed in preeclampsia.

[41] *Bruiners N, Dutta N, Guerrini V et al.* **The anti-tubercular activity of simvastatin is mediated by cholesterol-driven autophagy via the AMPK-mTORC1-TFEB axis**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32848049
ABSTRACT
The rise of drug-resistant tuberculosis (TB) poses a major risk to public health. Statins, which inhibit both cholesterol biosynthesis and protein prenylation branches of the mevalonate pathway, increase anti-tubercular antibiotic efficacy in animal models. However, the underlying molecular mechanisms are unknown. In this study, we used an in vitro macrophage infection model to investigate simvastatin's anti-tubercular activity by systematically inhibiting each essential branch of the mevalonate pathway and evaluating the effects of the branch-specific inhibitors on mycobacterial growth. The anti-tubercular activity of simvastatin used at clinically relevant doses specifically targeted the cholesterol biosynthetic branch rather than the prenylation branches of the mevalonate pathway. Using Western blot analysis and AMP/ATP measurements, we found that simvastatin treatment blocked activation of mechanistic target of rapamycin complex 1 (mTORC1), activated AMP-activated protein kinase (AMPK) through increased intracellular AMP:ATP ratios, and favored nuclear translocation of transcription factor EB (TFEB). These mechanisms all induce autophagy, which is anti-mycobacterial. The biological effects of simvastatin on the AMPK-mTORC1-TFEB-autophagy axis were reversed by adding exogenous cholesterol to the cells. Our data demonstrate that the anti-tubercular activity of simvastatin requires inhibiting cholesterol biosynthesis, reveal novel links between cholesterol homeostasis, AMPK- mTORC1-TFEB axis, and Mycobacterium tuberculosis infection control, and uncover new anti-tubercular therapy targets.

[42] *Hwang JT, Kim HJ, Choi HK et al.* **Butein Synergizes with Statin to Upregulate Low-Density Lipoprotein Receptor Through HNF1α-Mediated PCSK9 Inhibition in HepG2 Cells**. Journal of medicinal food 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32835593
ABSTRACT
Downregulation of the low-density lipoprotein (LDL) receptor (LDLR) can lead to hypercholesterolemia and related conditions, including cardiovascular diseases. Statins are a class of LDL cholesterol-lowering agents and are best-selling medications for patients at high risk of developing cardiovascular diseases. Indeed, statins upregulate LDLR and proprotein convertase subtilisin/kexin type 9a (PCSK9), leading to LDLR lysosomal degradation, which interferes with the attenuation of hypercholesterolemia. In the present study, butein was found to decrease extracellular PCSK9 levels by reducing its mRNA expression, which was attributable to butein-mediated downregulation of HNF1α in HepG2 cells. Butein-mediated PCSK9 inhibition further reversed LDLR protein synthesis inhibition, which possibly occurred through butein-mediated inhibition of LDLR degradation. When treated as a combination of butein and a statin, butein reduced statin-mediated enhancement of PCSK9 protein expression. This resulted in a synergistic enhancement of LDLR protein expression, whereas butein alone marginally increased LDLR protein expression. These findings suggest that butein, a novel PCSK9 inhibitor, may be a potential alternative or adjunct to statin treatment.

[43] *Zhang J, Yang P, Wang H et al.* **N-3 PUFAs inhibited hepatic ER stress induced by feeding of a high-saturated fat diet accompanied by the expression LOX-1**. The Journal of nutritional biochemistry 2020:108481.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32853678
ABSTRACT
Excessive consumption of saturated fat leads to non-alcoholic fatty liver disease (NAFLD), which is attenuated by supplementation of n-3 polyunsaturated fatty acids (PUFAs). Endoplasmic reticulum (ER) stress is crucial in the development of NAFLD, but how high-saturated fat diet (HFD) causes ER stress and NAFLD remains unclear. Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) is involved in hepatic ER stress. We aimed to explore the roles of LOX-1 in HFD-induced ER stress. Male Sprague-Dawley rats were fed an HFD without or with supplementation of fish oil for 16 weeks. The effects of n-3 PUFAs on hepatic ER stress degrees and the expression levels of LOX-1 were examined. Then human L02 hepatoma cells were treated with palmitate or palmitate and DHA to determine the ER stress and LOX-1 expression levels in vitro. After that the expression of LOX-1 in L02 cells was either knocked-down or overexpressed to analyze the roles of LOX-1 in palmitate-induced ER stress. The feeding of HFD induced NAFLD development and ER stress in the liver, and LOX-1 expressing level, which were all reversed by fish oil supplementation. In vitro, DHA treatment reduced the expression of LOX-1, and palmitate-induced ER stress. SiRNA-mediated knock-down of LOX-1 inhibited palmitate-induced ER stress, whereas overexpression of LOX-1 dramatically induced ER stress in L02 cells.LOX-1 is may critical for HFD-induced ER stress, and inhibition of its expression under the treatment of n-3 PUFAs could ameliorate HFD-induced NAFLD.

[44] *Alarfi H, Youssef LA, Salamoon M*. **A Prospective, Randomized, Placebo-Controlled Study of a Combination of Simvastatin and Chemotherapy in Metastatic Breast Cancer**. J Oncol 2020; 2020:4174395.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32849871

ABSTRACT

Preclinical studies support the anticancer activity of statins; however, the existing clinical evidence is inconsistent and not definitive. Our study aimed at evaluating a postulated cancer chemo-sensitizing effect of statin (simvastatin) in a cohort of metastatic breast cancer (MBC) patients. We designed a prospective, single-centered, randomized, double blinded, placebo-controlled trial that encompassed MBC patients with an ECOG Performance Status Scale ≤2 and scheduled to be treated with a chemotherapy regimen consisting of carboplatin and vinorelbine every 3 weeks at Al-Baironi Hospital, Damascus, Syria. Patients were enrolled between August 2011 and July 2012 and randomly allocated to receive a 15-day course of either simvastatin (40 mg) or placebo seven days prior to the first day of each chemotherapy cycle and then continued for eight days in each individual cycle. Primary endpoints were objective response rate (ORR) and toxicity, and the secondary endpoint was overall survival (OS). Eighty-two patients met the inclusion criteria and consented. ORR (35% vs. 32.5%) and predominant toxicity and grade ≥3 neutropenia (occurred in 30% vs. 40% of the patients) were not significantly different between simvastatin and placebo groups, respectively. Over a median follow-up of 44 months (range, 10-60), median OS was 15 months in the simvastatin group and 17 the in placebo group (hazard ratio (HR) = 1.16, 95% CI (0.70-1.91), P=0.57). Elevated baseline values of high-sensitivity C-reactive protein (hsCRP >10 mg/l), lactate dehydrogenase (LDH >480 U/L), and chemotherapy being ≥2(nd) line were significantly associated with shorter OS for the total cohort in both Univariate and multivariate analyses. Our data prove a safe profile of simvastatin at 40 mg per day combined with carboplatin and vinorelbine in MBC patients but without any beneficial increase of tumor sensitivity to chemotherapy. Moreover, we demonstrated a strong clinical advantage of baseline values of hsCRP and LDH as useful prognostic tools in MBC patients. This trial is registered with ISRCTN12964275.

[45] *Kose E, Kose M, Ozturk SI et al.* **Cascade screening and treatment of children with familial hypercholesterolemia in Turkey**. J Pediatr Endocrinol Metab 2020; 33:1251-1256.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32829317

ABSTRACT

Objectives Premature coronary artery disease is the most common preventable cause of death in developed countries, and familial hypercholesterolemia (FH) is the most common monogenetic disorder of lipid metabolism, predisposing for premature coronary artery. FH is the most common preventable cause of death in developed countries. In 2016, the national lipid screening program in school-age children has been started in Turkey. In this study, we aimed to evaluate the efficacy of lipid screening program, lipid-lowering treatments, and the challenges of treatments in children diagnosed with FH. Methods Patients diagnosed with FH in the pediatric metabolism outpatient clinic were retrospectively evaluated. Changes in lipid profile with dietary interventions and statin treatments were assessed. The results of cascade screening were analyzed. Results Fifty-one patients diagnosed with FH were enrolled in the study. Twenty-four (47.1%) were female. The mean age of the patients was 9.8 ± 3.2 years. Heterozygous LDLR gene mutation was detected in all patients. Three novel pathogenic

variations were revealed with the genetic investigation. Forty-one (80.4%) patients had high adherence to CHILD-2 dietary recommendations. The mean low-density lipoprotein cholesterol (LDL-C) level decreased by 14.5 ± 7.6% after dietary intervention. Parents refused to start statin treatment in 8 (15.7%) patients. Statin treatment was initiated to 22 (43.1%) patients. Mean LDL-C level decreased from 204.1 ± 19.1 mg/dL to 137.0 ± 13.1 mg/dL. In cascade screening, 7 (13.7%) parents without a diagnosis of FH were diagnosed with FH. After the screening program, statin treatment was initiated for 18 (35.3%) parents and 7 (16.3%) siblings. Conclusions We can conclude that screening for FH in children is crucial for diagnosing FH not only in children but also in their relatives. Although statins are safe and effective in achieving the target LDL-C level, we determined significant resistance for initiating statin treatment in patients.

[46] *Safari S, Amini M, Aminorroaya A, Feizi A*. **Patterns of changes in serum lipid profiles in prediabetic subjects: results from a 16-year prospective cohort study among first-degree relatives of type 2 diabetic patients**. Lipids in health and disease 2020; 19:193.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32829710

ABSTRACT

BACKGROUND: Lipid abnormality pervasively is associated with the risk of type 2 diabetes mellitus. To the best of our knowledge, there is no study that has examined the longitudinal changes in a wide range of serum lipid profiles in prediabetic subjects in association with the risk of developing type 2 diabetes mellitus in the future. This study aimed to identify the patterns of changes in lipid profiles over time in prediabetic patients and to classify these subjects in order to highlight which patients are at high risk for future diabetes. METHODS: This prospective 16-year (2003-2019) cohort study was conducted among 1228 prediabetic subjects. The study subjects were followed, and the changes in their lipid profiles, including triglycerides, cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, were evaluated. The latent Markov model was used for data analysis. RESULTS: The mean (standard deviation) age of subjects was 44.0 (6.8) years, and 73.6% of them were female. The latent Markov model identified two latent states of subjects in terms of changes in lipid profiles: a low tendency to progress diabetes / high tendency to progress diabetes (74, 26%). The latent Markov model showed that the transition probability from a "low tendency to progress diabetic" state to a "high tendency to progress diabetic" state was lower than the transition probability from "high tendency to progress diabetic" state to "low tendency to progress diabetic" state. CONCLUSIONS: The present study showed that more than half of the first-degree relatives of T2DM had approximately normal lipid profiles and that these patients are more inclined to transition from a higher- to a lower-tendency diabetic state. These findings confirm the value of regular screening of first-degree relatives of T2DM. Moreover, preventive intervention strategies are recommended to reduce their risk of developing T2DM.

[47] *Quiroga-Padilla PJ, Gaete PV, Mendivil CO*. **[Familial chylomicronemia]**. Medicina 2020; 80:348-358.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32841138

ABSTRACT

Familial chylomicronemia is a disease in which a genetic mutation affects the ability of the organism to metabolize triglycerides bound to lipoproteins, causing extremely high plasma triglycerides and associated consequences. The most frequent complication is acute

pancreatitis, which may lead to multiorganic failure or pancreatic insufficiency. Familial chylomicronemia also exerts a profound negative impact on quality of life, social relationships and professional development. The gene most frequently affected is lipoprotein lipase-1 gene (LPL), the enzyme in charge of hydrolyzing circulating triglycerides for tissue uptake. Mutations in other genes regulating maturation, transport or polymerization (eg. APOC2, APOAV, LMF-1, GPIHBP-1) of lipoprotein lipase-1, may also be involved. However, in about 30% of patients the causal variant is not identified. Familial chylomicronemia should be suspected in patients with severe hypertriglyceridemia with poor response to conventional treatment, or accompanied by eruptive xanthomas, lipemia retinalis or abdominal pain. The availability of risk scores and genetic tests should facilitate its opportune detection and management. Nutritional therapy is based on a very-low-fat diet with adequate supply of lipid-soluble vitamins and essential fatty acids, plus avoidance of alcohol consumption. Current pharmacological treatment may include fibrates and omega-3 fatty acids but prioritizes biotechnological agents targeting the molecular disturbances of the disease. These include an antisense oligonucleotide against apoC-III (volanesorsen), a monoclonal antibody against angiopoietin-like protein-3 (evinacumab), and other agents currently in development.

[48] *Bayona A, Arrieta F, Rodríguez-Jiménez C et al.* **Loss-of-function mutation of PCSK9 as a protective factor in the clinical expression of familial hypercholesterolemia: A case report**. Medicine (Baltimore) 2020; 99:e21754.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32846800

ABSTRACT
RATIONALE: Proprotein convertase subtilisin/kexin 9 or PCSK9 is a protein whose main function is to regulate the number of low-density lipoprotein receptors (LDLR) present on the cell surface. Loss-of-function mutations in PCSK9 have been related to low LDL-cholesterol levels and a decrease in the risk of cardiovascular events. PATIENT CONCERNS: We present the case of a 27-year-old woman, offspring of a patient with familial homozygous hypercholesterolemia, who presented with mild-moderate hypercholesterolemia. DIAGNOSIS: Genetic analysis was performed by next generation sequencing using a customized panel of 198 genes. Sanger sequencing was used to confirm the presence of the variants of interest. The genetic analysis showed a pathogenic heterozygous mutation in LDLR [exon 6:c.902A>G:p(Asp301Gly)], as well as a loss-of-function heterozygous variant in PCSK9 [exon1:c.137 G>T:p.(Arg46Leu)]. The genetic analysis of the index case's mother revealed compound heterozygosity for 2 different mutations in LDLR [c.902A>G:p.(Asp301Gly); c.1646G>T:p.(Gly549Val)] in exon 6 and in exon 11, respectively, and the same loss-of-function variant in PCSK9 that had been found in her daughter [(PCSK9:exon1:c.137G>T:p.(Arg46Leu)]. The maternal grandfather of the index case presented the same genetic variants as his granddaughter. INTERVENTIONS: The index case did not receive any specific treatment for hypercholesterolemia. The loss-of-function variant in PCSK9 protected her from higher LDL-cholesterol levels, provided she kept partial activity of the LDLR. In her mother, instead, a PCSK9 inhibitor was tried but failed to achieve lipid control. The reason for this may be the complete absence in LDL receptor activity. LDL apheresis was started afterwards, resulting in adequate lipid level control. OUTCOMES: To the date, the index case has achieved to maintain adequate total and LDL-cholesterol levels without any other intervention. She has had no known cardiovascular complication. LESSONS: Loss-of-function mutations in PCSK9 could protect from developing more severe forms of

hypercholesterolemia. The finding of these mutations (LDLR-PCSK9) in three consecutive generations could imply an adaptive mechanism against the development of hypercholesterolemia.

[49] *Vergallo R, Crea F*. **Atherosclerotic Plaque Healing**. The New England journal of medicine 2020; 383:846-857.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32846063
ABSTRACT

[50] *D'Erasmo L, Commodari D, Di Costanzo A et al.* **Evolving trend in the management of heterozygous familial hypercholesterolemia in Italy: A retrospective, single center, observational study**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32830020
ABSTRACT
BACKGROUND AND AIMS: The effective reduction of LDL-C in patients with heterozygous familial hypercholesterolemia (HeFH) is crucial to reduce their increased cardiovascular risk. Diagnostic and therapeutic (PCSK9 inhibitors) tools to manage HeFH improved in recent years. However, the impact of these progresses in ameliorating the contemporary real-world care of these patients remains to be determined. Aim of this study was to assess the evolution of treatments and LDL-C control in a cohort of HeFH patients in Italy. METHODS AND RESULTS: Four hundred six clinically diagnosed HeFH followed in a single, tertiary lipid centre were included in this survey. Data on lipid levels and medications were collected at baseline and during a median 3-year follow-up. At baseline, 19.8% of patients were receiving conventional high-potency lipid lowering therapies (LLT) and this percentage increased up to 50.8% at last visit. The knowledge of results of molecular diagnosis was associated with a significant increase in treatment intensity and LDL-C lowering. Nevertheless, the new LDL-C target (<70 mg/dl) was achieved only in 3.6% of HeFH patients under conventional LLTs and this proportion remained low (2.9%) also in those exposed to maximal conventional LLT. In 51 patients prescribed with PCSK9 inhibitors, 64.6% and 62.1% reached LDL-C<70 mg/dl at 3- and 12-month follow-up, respectively. CONCLUSIONS: Although treatments of HeFH improved over time, LDL-C target achievement with conventional LLT remains poor, mainly among women. The use of molecular diagnosis and even more the prescription of PCSK9i may improve LDL-C control in these patients.

[51] *Abeyratne T, Perera R, Fernando S*. **Obesity and cardiovascular risk among Sri Lankan adolescents: Association of adipokines with anthropometric indices of obesity and lipid profile**. Nutrition 2020; 78:110942.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32854019
ABSTRACT
OBJECTIVES: Obesity and being overweight among adolescents pose a significant problem and are known to cause several physical and biochemical disorders during adulthood. This study was designed to identify the biomarkers of obesity and describe associations with selected metabolic disorders of obesity among Sri Lankan adolescents. METHODS: The present study compared the characteristics of obese (n = 121) and normal weight (n = 263) adolescents, including sociodemographic, anthropometric, and selected biochemical parameters (e.g., lipid profile, serum leptin, adiponectin, and high-sensitivity C-reactive protein

[hs-CRP]). An enzyme-linked immunosorbent assay technique and fully automated clinical chemistry analyzer were used to analyze the biochemical parameters among adolescents ages 10 to 16. RESULTS: The mean age of the sample was 13.1 y [standard deviation (SD): 1.9 y], and the male-to-female ratio 1:1. The mean weight of obese children was 55.70 kg (SD: 14.82 kg), which was significantly higher than that of children of normal weight [41.63 kg (SD: 7.88 kg)]. Total cholesterol, triacylglycerol, and low-density lipoprotein cholesterol levels were significantly higher (P = 0.000) among obese adolescents compared with those of normal weight. High-density lipoprotein cholesterol was significantly lower among obese adolescents. Serum leptin and hs-CRP were higher among obese adolescents, but adiponectin was lower. In the multivariate analysis, owing to confounding effects among the tested adipokines, serum leptin was the only predictor of an abnormal lipid profile. CONCLUSIONS: Serum leptin, adiponectin, and hs-CRP were found to be reliable biomarkers of predicting adiposity related metabolic disorders in adolescents. Obese adolescents showed disorders in the lipid metabolism with abnormal lipid profiles compared with children of normal weight.

[52] *Mickiewicz A, Kreft E, Kuchta A et al.* **The Impact of Lipoprotein Apheresis on Oxidative Stress Biomarkers and High-Density Lipoprotein Subfractions**. Oxidative medicine and cellular longevity 2020; 2020:9709542.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32832012

ABSTRACT

Lipoprotein apheresis (LA) treatment results in a substantial reduction of low-density lipoprotein- (LDL-) cholesterol and lipoprotein(a) concentrations, which consequently decreases the rate of cardiovascular events. The additional benefit of LA may be associated with its impact on the composition and quality of high-density lipoprotein (HDL) particles, inflammation, and oxidative stress condition. To verify the effects of LA procedure, the current study is aimed at analyzing the effect of a single apheresis procedure with direct hemadsorption (DALI) and cascade filtration (MONET) on oxidative stress markers and HDL-related parameters. The study included eleven patients with familial hypercholesterolemia and hyperlipoproteinemia(a) treated with regular LA (DALI or MONET). We investigated the pre- and postapheresis concentration of the lipid-related oxidative stress markers 8-isoPGF2, oxLDL, TBARS, and PON-1. We also tracked potential changes in the main HDL apolipoproteins (ApoA-I, ApoA-II) and cholesterol contained in HDL subfractions. A single session of LA with DALI or MONET techniques resulted in a similar reduction of lipid-related oxidative stress markers. Concentrations of 8-isoPGF2 and TBARS were reduced by ~60% and ~30%, respectively. LA resulted in a 67% decrease in oxLDL levels along with a ~19% reduction in the oxLDL/ApoB ratio. Concentrations of HDL cholesterol, ApoA-I, ApoA-II, and PON-1 activity were also reduced by LA sessions, with more noticeable effects seen in the MONET technique. The quantitative proportions between HDL(2) and HDL(3) cholesterol did not change significantly by both methods. In conclusion, LA treatment with MONET or DALI system has a small nonselective effect on lowering HDL particles without any changes in the protein composition of these particles. Significant reduction in the level of oxidative stress parameters and less oxidation of LDL particles may provide an additional benefit of LA therapy.

[53] *Hahn HJ, Debnath A*. **In Vitro Evaluation of Farnesyltransferase Inhibitor and its Effect in Combination with 3-Hydroxy-3-Methyl-Glutaryl-CoA Reductase Inhibitor against Naegleria fowleri**. Pathogens 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32842691
ABSTRACT
Free-living amoeba Naegleria fowleri causes a rapidly fatal infection primary amebic meningoencephalitis (PAM) in children. The drug of choice in treating PAM is amphotericin B, but very few patients treated with amphotericin B have survived PAM. Therefore, development of efficient drugs is a critical unmet need. We identified that the FDA-approved pitavastatin, an inhibitor of HMG Co-A reductase involved in the mevalonate pathway, was equipotent to amphotericin B against N. fowleri trophozoites. The genome of N. fowleri contains a gene encoding protein farnesyltransferase (FT), the last common enzyme for products derived from the mevalonate pathway. Here, we show that a clinically advanced FT inhibitor lonafarnib is active against different strains of N. fowleri with EC(50) ranging from 1.5 to 9.2 μM. A combination of lonafarnib and pitavastatin at different ratios led to 95% growth inhibition of trophozoites and the combination achieved a dose reduction of about 2- to 28-fold for lonafarnib and 5- to 30-fold for pitavastatin. No trophozoite with normal morphology was found when trophozoites were treated for 48 h with a combination of 1.7 μM each of lonafarnib and pitavastatin. Combination of lonafarnib and pitavastatin may contribute to the development of a new drug regimen for the treatment of PAM.

[54] *Zhaori G*. **RNAi technique, how far is it from pediatrics?** Pediatr Investig 2017; 1:40-46.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32851217
ABSTRACT
The new technology of ribonucleic acid interference (RNAi) or small/short interfering RNA (siRNA) can be used to reduce expression of genes in a sequence specific manner, and thereby can treat various diseases caused by expression or overexpression of genes. Phase 1 and phase 2 clinical studies on application of this technology to treat diseases have demonstrated efficacy and safety of this approach in a few specialties/subspecialties. However, no clinical trials have been reported in the fields of pediatrics. This article aimed to describe very briefly what the RNAi technique is, examples of demonstration of the efficacy and safety of RNAi techniques in a few different fields of clinical medicine, and to encourage pediatricians and pediatric researchers to actively participate in studies on this new therapeutic approach for treatment of various pediatric diseases.

[55] *Engeda JC, Lhachimi SK, Rosamond WD et al.* **Projections of incident atherosclerotic cardiovascular disease and incident type 2 diabetes across evolving statin treatment guidelines and recommendations: A modelling study**. PLoS medicine 2020; 17:e1003280.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32845900
ABSTRACT
BACKGROUND: Experimental and observational research has suggested the potential for increased type 2 diabetes (T2D) risk among populations taking statins for the primary prevention of atherosclerotic cardiovascular disease (ASCVD). However, few studies have directly compared statin-associated benefits and harms or examined heterogeneity by population subgroups or assumed treatment effect. Thus, we compared ASCVD risk reduction and T2D incidence increases across 3 statin treatment guidelines or recommendations among

adults without a history of ASCVD or T2D who were eligible for statin treatment initiation. METHODS AND FINDINGS: Simulations were conducted using Markov models that integrated data from contemporary population-based studies of non-Hispanic African American and white adults aged 40-75 years with published meta-analyses. Statin treatment eligibility was determined by predicted 10-year ASCVD risk (5%, 7.5%, or 10%). We calculated the number needed to treat (NNT) to prevent one ASCVD event and the number needed to harm (NNH) to incur one incident case of T2D. The likelihood to be helped or harmed (LHH) was calculated as ratio of NNH to NNT. Heterogeneity in statin-associated benefit was examined by sex, age, and statin-associated T2D relative risk (RR) (range: 1.11-1.55). A total of 61,125,042 U.S. adults (58.5% female; 89.4% white; mean age = 54.7 years) composed our primary prevention population, among whom 13-28 million adults were eligible for statin initiation. Overall, the number of ASCVD events prevented was at least twice as large as the number of incident cases of T2D incurred (LHH range: 2.26-2.90). However, the number of T2D cases incurred surpassed the number of ASCVD events prevented when higher statin-associated T2D RRs were assumed (LHH range: 0.72-0.94). In addition, females (LHH range: 1.74-2.40) and adults aged 40-50 years (LHH range: 1.00-1.14) received lower absolute benefits of statin treatment compared with males (LHH range: 2.55-3.00) and adults aged 70-75 years (LHH range: 3.95-3.96). Projected differences in LHH by age and sex became more pronounced as statin-associated T2D RR increased, with a majority of scenarios projecting LHHs < 1 for females and adults aged 40-50 years. This study's primary limitation was uncertainty in estimates of statin-associated T2D risk, highlighting areas in which additional clinical and public health research is needed. CONCLUSIONS: Our projections suggest that females and younger adult populations shoulder the highest relative burden of statin-associated T2D risk.

[56] *Han YL, Ma YY, Su GH et al.* **[Efficacy and safety of alirocumab versus ezetimibe in high cardiovascular risk Chinese patients with hyperlipidemia: ODYSSEY EAST Study-Chinese sub-population analysis]**. Zhonghua xin xue guan bing za zhi 2020; 48:593-599.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32842270

ABSTRACT

Objective: To compare the efficacy and safety profile of alirocumab (PCSK9 inhibitor) versus ezetimibe on top of maximally tolerated statin dose in high cardiovascular risk Chinese patients with hyperlipidemia. Methods: The ODYSSEY EAST study was a randomized, double-blinded, double dummy, active-control, parallel group, multi-centers clinical trial, the Chinese sub-population included 456 patients with hyperlipidemia and high cardiovascular risk on maximally tolerated statin dose. Patients were randomized (2∶1) to receive the subcutaneous injection of alirocumab (75 mg Q2W; with dose up titration to 150 mg Q2W at week 12 if low-density lipoprotein cholesterol (LDL-C) was ≥1.81 mmol/L at week 8) or the oral administration of ezetimibe (10 mg daily) for 24 weeks. The primary endpoint was percentage change in calculated LDL-C from baseline to week 24. Key secondary efficacy endpoints included percentage change from baseline to week 12 or 24 in LDL-C (week 12) and other lipid parameters, including apolipoprotein (Apo) B, non-high-density lipoprotein cholesterol (non-HDL-C), TC, lipoprotein(a) (Lp(a)), HDL-C, fasting triglycerides (TG), and Apo A1, and the proportion of patients reaching LDL-C<1.81 mmol/L at week 24. Safety profile of therapeutic drugs was also assessed during the treatment period. Results: The mean age of 456 Chinese patients was (59.5±10.9) years, 341(74.8%) patients were male, 303 patients (66.4%) in alirocumab group and 153 patients (33.5%) in ezetimibe group. Demographic characteristics,

disease characteristics, and lipid parameters at baseline were similar between the two groups. LDL-C was reduced more from baseline to week 12 and 24 in alirocumab group versus ezetimibe group, the difference of their least-squares mean (standard error) percent change were(-35.2±2.2)% and (-36.9±2.5)% (both P<0.001). At 12 weeks, alirocumab had significant reduction on Lp(a), Apo B, total cholesterol and non HDL-C, the difference of their least-squares mean (standard error) percent change were (-40.3±2.8)%, (-27.7±1.8)%, (-19.6±1.5)% and (-27.7±1.9)%, respectively (all P<0.001). At 24 weeks, the percent of patients who reached LDL-C<1.81 mmol/L and LDL-C<1.42 mmol/L was significantly higher in alirocumab group (85.3% and 70.5%) than in ezetimibe group (42.2% and 17.0%, both P<0.001), and alirocumab use was also associated with significant reduction on Lp(a), Apo B, total cholesterol and non HDL-C, the difference of their least-squares mean (standard error) percent change were (-37.2±2.8)%, (-29.1±2.0)%, (-21.6±1.6)% and (-29.6±2.2)%, respectively (all P<0.001). The incidence of treatment related adverse events was similar between the two treatment groups (223/302 patients (73.8%) in alirocumab group and 109/153 patients (71.2%) in ezetimibe group). Respiratory infection, urinary infection, dizziness and local injection-site reactions were the most frequently reported adverse events. Conclusions: In high cardiovascular risk patients with hyperlipidemia from China on maximally tolerated statin dose, the reduction of LDL-C induced by alirocumab is more significant than that induced by ezetimibe. Both treatments were generally safe during the observation period of study.

[57] *Xu JJ, Jiang L, Song Y et al.* **[Related factors and the long-term outcome after percutaneous coronary intervention of premature acute myocardial infarction]**. Zhonghua xin xue guan bing za zhi 2020; 48:655-660.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32847321

ABSTRACT

Objective: To explore the related factors of premature acute myocardial infarction(AMI), and to compare the the long-term outcomes in patients with and without premature AMI after percutaneous coronary intervention (PCI). Methods: This study was a prospective cohort study.From January 2013 to December 2013, 10 724 consecutive patients with coronary heart disease undergoing PCI in Fuwai Hospital were enrolled. Among them 1 920 patients with the diagnosis of AMI were divided into two groups: premature AMI (man≤50 years old, woman≤60 years old) and non-premature AMI. The baseline characteristics were collected, and multivariate logistic regression was uesed to analysis the related factors of premature AMI. The clinical outcomes, including the major adverse cardiovascular and cerebrovascular events(MACCE) which was the composite of cardiac death, myocardial infarction, revascularization, stroke and stent thrombosis, as well as bleeding events, during hospitalization, at 2 years and 5 years follow-up were analyzed. Results: A total of 1 920 AMI patiens were included(age was (56.5±11.3) years old), with 1 612(84.0%) males. There were statistically significant differences between the two groups in gender, body mass index, blood lipid, complications, inflammatory markers, etc (all P<0.05). Multivariate logistic regression analysis showed body mass index(OR=1.06, 95%CI 1.01-1.10, P<0.01), triglyceride(OR=1.47, 95%CI 1.14-1.90, P<0.01), serum uric acid level(OR=1.02, 95%CI 1.01-1.04, P<0.01), high density lipoprotein cholesterol level(OR=0.33, 95%CI 0.14-0.78, P=0.01) and history of hypertension(OR=0.72, 95%CI 0.56-0.93, P=0.01) were independent related factors of premature AMI. The incidence of all-cause death and cardiac death were lower during hospitalization, at 2 years and 5 years follow-up in the premature AMI group than in non-

premature AMI group(all P<0.05). In the premature AMI group, the incidence of MACCE and stroke was lower, with more bleeding events in 5 years follow-up(all P<0.05). Conclusions: Metabolic abnormalities, including high BMI, high triglyceride level and high serum uric acid, low high-density lipoprotein cholesterol level are the related factor of premature AMI. The incidence of ischemic events in patients with premature AMI is lower, while the incidence of bleeding events is higher than non-premature AMI patients.

[58] *Wen Y, Wang G, Chen HD et al.* **[Total cholesterol and the risk of primary liver cancer in Chinese males: a prospective cohort study]**. Zhonghua Yu Fang Yi Xue Za Zhi 2020; 54:753-759.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32842298
ABSTRACT
Objective: To investigate the association between total cholesterol (TC) and primary liver cancer in Chinese males. Methods: Since May 2006, all the male workers, including the employees and the retirees in Kailuan Group were recruited in the Kailuan male dynamic cohort study. Information about demographics, medical history and TC levels was collected at the baseline interview, as well as information on newly-diagnosed primary liver cancer cases during the follow-up period. A total of 110 612 males were recruited in the cohort by 31 December 2015. TC levels were divided into four categories by quartile (<4.27, 4.27-4.90, 4.90-5.56 and ≥5.56 mmol/L), with the first quartile group serving as the referent category. Cox proportional hazards regression model was used to evaluate the association between TC levels and primary liver cancer risk. Results: By December 31, 2015, a follow-up of 861 711.45 person-years was made with a median follow-up period of 8.83 years. During the follow-up, 355 primary liver cancer cases were identified. Compared with the first quartile, the HR of incident primary liver cancer among participants with the second, third and highest quartile TC levels were 0.76 (95%CI: 0.58-1.01), 0.59 (95%CI: 0.43-0.79), and 0.36 (95%CI: 0.25-0.52), respectively after adjusting for age, educational level, income level, smoking status, drinking status, body mass index, and HBsAg status (P(for trend)<0.001). Subgroup analyses found that the association between TC levels and primary liver cancer was robust (all P(for trend)<0.05). The results didn't change significantly after exclusion of newly-diagnosed cases within the first 2 years, males with history of cirrhosis or subjects who took antihyperlipidemic drugs, participants with higher TC levels had a lower risk of primary liver cancer (all P(for trend)<0.05) and HR(95%CI) of incident primary liver cancer among participants with the highest quartile TC levels were 0.41 (0.28-0.61), 0.36 (0.25-0.53) and 0.38 (0.26-0.54), respectively. Conslusion: In this large prospective study, we found that baseline TC levels were inversely associated with primary liver cancer risk, and low TC level might increase the risk of primary liver cancer.

[59] *Sun XY, Ma F, Tian PF et al.* **[The metabolism of blood glucose and lipid in breast cancer patients after the first chemotherapy]**. Zhonghua Zhong Liu Za Zhi 2020; 42:580-585.
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ABSTRACT
Objective: To analyze the metabolism of blood glucose and lipid in breast cancer patients after the first chemotherapy. Methods: Breast cancer patients who received chemotherapy for the first time from December 2016 to January 2020 were collected in our hospital, and their blood

glucose and lipid levels were monitored. Patients were grouped according to different treatment plans. Non-parametric rank sum test was used for statistical analysis on SPSS software. Results: There were 1 356 female breast cancer patients were enrolled, blood glucose and lipid levels were compared before and after chemotherapy. Our results showed that baseline medium blood glucose was 5.2 mmol/L, lower than 5.3 mmol/L after chemotherapy ($P<0.05$). The baseline triglyceride (TG) was 1.2 mmol/L, lower than 1.6 mmol/L after chemotherapy ($P<0.05$). The baseline small dense low-density lipoprotein (sdLDL) was 0.7 mmol/L, lower than 0.8 mmol/L after chemotherapy ($P<0.05$). The baseline high density lipoprotein (HDL) was 1.3 mmol/L, higher than 1.2 mmol/L after chemotherapy ($P<0.05$). Patients' menstrual status and body mass index were related with blood glucose, TG, LDL and sdLDL (all $P< 0.05$). Conclusions: Abnormal metabolism of blood glucose and lipid are observed in breast cancer patients after the first chemotherapy. More awareness of cardiovascular disease in breast cancer patients might ensure their overall clinical benefits.