[1] *Wei LL, Ma N, Wu KY et al.* **Protective Role of C3aR (C3a Anaphylatoxin Receptor) Against Atherosclerosis in Atherosclerosis-Prone Mice**. Arteriosclerosis, thrombosis, and vascular biology 2020; 40:2070-2083.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762445

ABSTRACT

OBJECTIVE: Emerging evidence suggests that C3aR (C3a anaphylatoxin receptor) signaling has protective roles in various inflammatory-related diseases. However, its role in atherosclerosis has been unknown. The purpose of the study was to investigate the possible protective role of C3aR in aortic atherosclerosis and explore molecular and cellular mechanisms involved in the protection. Approach and Results: C3ar(-/-)/Apoe(-/-) mice were generated by cross-breeding of atherosclerosis-prone Apoe(-/-) mice and C3ar(-/-) mice. C3ar(-/-)/Apoe(-/-) mice and Apoe(-/-) mice (as a control) underwent high-fat diet for 16 weeks were assessed for (1) atherosclerotic plaque burden, (2) aortic tissue inflammation, (3) recruitment of CD11b(+) leukocytes into atherosclerotic lesions, and (4) systemic inflammatory responses. Compared with Apoe(-/-) mice, C3ar(-/-)/Apoe(-/-) mice developed more severe atherosclerosis. In addition, C3ar(-/-)/Apoe(-/-) mice have increased local production of proinflammatory mediators (eg, CCL2 [chemokine (C-C motif) ligand 2], TNF [tumor necrosis factor]-α) and infiltration of monocyte/macrophage in aortic tissue, and their lesional macrophages displayed an M1-like phenotype. Local pathological changes were associated with enhanced systemic inflammatory responses (ie, elevated plasma levels of CCL2 and TNF-α, increased circulating inflammatory cells). In vitro analyses using peritoneal macrophages showed that C3a stimulation resulted in upregulation of M2-associated signaling and molecules, but suppression of M1-associated signaling and molecules, supporting the roles of C3a/C3aR axis in mediating anti-inflammatory response and promoting M2 macrophage polarization. CONCLUSIONS: Our findings demonstrate a protective role for C3aR in the development of atherosclerosis and suggest that C3aR confers the protection through C3a/C3aR axis-mediated negative regulation of proinflammatory responses and modulation of macrophage toward the anti-inflammatory phenotype.

[2] *Wang G, Zhang X, Lu X et al.* **Fish oil supplementation attenuates cognitive impairment by inhibiting neuroinflammation in STZ-induced diabetic rats**. Aging 2020; 12:15281-15289.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32756005

ABSTRACT

Type 2 diabetes mellitus (T2DM) markedly impairs human health. During T2DM development, some patients experience cognitive dysfunction and behavioral deficits, which are characterized by neuronal injury and memory loss. It has been reported that the incidence of dementia in middle-aged and elderly patients with diabetes is significantly higher than that in normal elderly patients. Currently, the pathogenesis of cognitive dysfunction in diabetes remains unknown, and there is no standard or specific method to diagnose the disease in clinical practice. Evidence has shown that fish oil (FO) can alleviate depressive-like behaviors by attenuating neuroinflammation in a rat model, and improve cognitive dysfunction by inhibiting apoptosis. Therefore, it is reasonable to speculate that FO may reduce cognitive impairment by attenuating neuroinflammation in diabetic rats. In the present study, we investigated the effects of FO supplementation on cognitive dysfunction in a streptozotocin-induced diabetic rat model. FO administration for 10 weeks improved spatial learning and

memory as evaluated by performance in the Morris water maze (MWM). Besides, FO significantly improved the morphology of neurons in the hippocampus and cortex of diabetic rats and reduced the neuronal nuclear condensation. Moreover, FO decreased the mRNA expression of IL-1β, IL -6, and TNF-α and increased the mRNA expression of IL-4 and IL-10 in the cortex and hippocampus. FO also attenuated the brain inflammatory cascade and simultaneously reduced diabetes-induced oxidative stress. In addition, FO increased the protein expression of Nrf2 and HO-1 in cortex and hippocampus of diabetic rats. These results provide a novel horizon for the study of neuroprotective effect of FO and further clarify the connections among inflammation, oxidative stress and diabetes-induced cognitive impairment.

[3] *Sun J, Cheng W, Fan Z, Zhang X*. **Influence of high-intensity intermittent training on glycolipid metabolism in obese male college students**. Ann Palliat Med 2020; 9:2013-2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762224
ABSTRACT
BACKGROUND: Obesity is a chronic metabolic disease that increases the risk of developing health problems including respiratory disease, hypertension, hyperlipidemia, diabetes, and coronary heart disease. In college students, as well as impacting physical health, obesity can also affect mental health and even students' future careers. Aerobic exercise is an effective way of achieving weight loss; however, for some students, it cannot be maintained over the long term. This study aimed to observe and analyze the influence of high-intensity intermittent training on glycolipid metabolism in obese male college students. METHODS: A total of 300 obese male college students were enrolled in the study and were randomly divided into the study group and the control group (150 cases in each group). Over 12 weeks, the control group was given routine aerobic exercise intervention, while the study group was given high-intensity intermittent training. The blood sugar level, blood lipid level, and body measurements of the students were measured before and after intervention and compared between the two groups. RESULTS: After 12 weeks of intervention, the body weight, waist circumference, waist-hip ratio, body mass index (BMI), body fat rate (BFR), serum level of insulin, low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG) of the college students were significantly lower than before intervention, and the differences were statistically significant ($P<0.05$). There were no significant differences in body weight, waist circumference, waist-hip ratio, BMI, or BFR between the two groups ($P>0.05$). The study group had significantly lower serum levels of TC, TG, and insulin than the control group, and the differences were statistically significant ($P<0.05$). CONCLUSIONS: Aerobic exercise and high-intensity intermittent training both significantly improved the body shape of obese male college students. However, high-intensity intermittent training improved the glycolipid metabolism of obese male college students to a greater extent than aerobic exercise did.

[4] *Rtail R, Maksymova O, Illiashenko V et al.* **Improvement of Skeletal Muscle Regeneration by Platelet-Rich Plasma in Rats with Experimental Chronic Hyperglycemia**. BioMed research international 2020; 2020:6980607.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32766312
ABSTRACT
Herein, the structural effect of autologous platelet-rich plasma (PRP) on posttraumatic skeletal muscle regeneration in rats with chronic hyperglycemia (CH) was tested. 130 white laboratory

male rats divided into four groups (I-control; II-rats with CH; III-rats with CH and PRP treatment; and IV-rats for CH confirmation) were used for the experiment. CH was simulated by streptozotocin and nicotinic acid administration. Triceps surae muscle injury was reproduced by transverse linear incision. Autologous PRP was used in order to correct the possible negative CH effect on skeletal muscle recovery. On the 28th day after the injury, the regenerating muscle fiber and blood vessel number in the CH+PRP group were higher than those in the CH rats. However, the connective tissue area in the CH group was larger than that in the CH+PRP animals. The amount of agranulocytes in the regenerating muscle of the CH rats was lower compared to that of the CH+PRP group. The histological analysis of skeletal muscle recovery in CH+PRP animals revealed more intensive neoangiogenesis compared to that in the CH group. Herewith, the massive connective tissue development and inflammation signs were observed within the skeletal muscle of CH rats. Obtained results suggest that streptozotocin-induced CH has a negative effect on posttraumatic skeletal muscle regeneration, contributing to massive connective tissue development. The autologous PRP injection promotes muscle recovery process in rats with CH, shifting it away from fibrosis toward the complete muscular organ repair.

[5] *Nelson M*. **Absolute cardiovascular disease risk and the use of the Australian cardiovascular disease risk calculator**. Australian journal of general practice 2020; 49:471-473.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32738857
ABSTRACT
BACKGROUND: Primary prevention of cardiovascular disease (CVD) has been traditionally guided by individual risk factors such hypertension and hypercholesterolaemia. An absolute risk-based approach is more effective. OBJECTIVE: The aim of this article is to outline the superiority of an absolute risk-based approach when compared with individual risk factor management for the primary prevention of CVD, and to elaborate on the derivation and use of the Australian absolute CVD risk calculator. DISCUSSION: An absolute risk-based approach is superior to the traditional individual risk factor approach when identifying which patients would benefit most from the prescription of blood pressure-lowering and lipid-lowering medications.

[6] Feingold KR. Role of Glucose and Lipids in the Atherosclerotic Cardiovascular Disease of Patients with Diabetes. In: Endotext. Edited by: Feingold KR, Anawalt B, Boyce A *et al.* South Dartmouth (MA): MDText.com, Inc.

[7] *El-Say KM, Ahmed TA, Ahmed OAA, Elimam H*. **Enhancing the Hypolipidemic Effect of Simvastatin in Poloxamer-Induced Hyperlipidemic Rats via Liquisolid Approach: Pharmacokinetic and Pharmacodynamic Evaluation**. AAPS PharmSciTech 2020; 21:223.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32749629
ABSTRACT
This study aimed to enhance the dissolution of simvastatin (SMV) through its formulation in liquisolid tablets (LSTs) to improve its bioavailability and hypolipidemic activity after oral administration. SMV-LSTs were optimized using Box-Behnken design to maximize the rate and extent of SMV dissolution. The optimized SMV-LST was evaluated for pharmacokinetic parameters and potential hypolipidemic activity on induced hyperlipidemic rats. The dissolution parameters revealed a shortening of mean dissolution time from 10.99 to 6.82 min, increasing

of dissolution rate during the first 10 min from 1253.15 to 1667.31 μg/min, and enhancing of dissolution efficiency after 60 min from 71.92 to 86.93% for SMV-LSTs versus the commercial SMV tablets. The obtained data reflected an improvement in the relative bioavailability of SMV with 148.232% which was confirmed by the significant reduction of the levels of circulating total cholesterol, triglycerides that reached the normal level after 12 h. In particular, the optimized SMV-LSTs reduced serum low-density lipoproteins (LDL) by 44.6% which was significantly different from the commercial SMV tablets. In contrast, the level of serum high-density lipoprotein (HDL) was significantly augmented after 4 h in rats treated with the optimized SMV-LSTs by 47.6%. Finally, the optimized SMV-LSTs showed a significant lower atherosclerotic index value which could maximize its potential in decreasing the risk of coronary disease and atherosclerosis. Overall enhancement in pharmacokinetics and pharmacodynamics in comparison with the commercial tablets confers the potential of the liquisolid approach as a promising alternative for improved oral bioavailability, hypolipidemic, and cardioprotective effects of SMV. Graphical abstract.

[8] *Das UN*. **Bioactive Lipids as Mediators of the Beneficial Action(s) of Mesenchymal Stem Cells in COVID-19**. Aging and disease 2020; 11:746-755.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32765941
ABSTRACT
It is proposed that the beneficial action of mesenchymal stem cells (MSCs) in COVID-19 and other inflammatory diseases could be attributed to their ability to secrete bioactive lipids (BALs) such as prostaglandin E2 (PGE2) and lipoxin A4 (LXA4) and other similar BALs. This implies that MSCs that have limited or low capacity to secrete BALs may be unable to bring about their beneficial actions. This proposal implies that pretreatment of MSCs with BALs enhance their physiological action or improve their (MSCs) anti-inflammatory and disease resolution capacity to a significant degree. Thus, the beneficial action of MSCs reported in the management of COVID-19 could be attributed to their ability to secrete BALs, especially PGE2 and LXA4. Since PGE2, LXA4 and their precursors AA (arachidonic acid), dihomo-gamma-linolenic acid (DGLA) and gamma-linolenic acid (GLA) inhibit the production of pro-inflammatory IL-6 and TNF-α, they could be employed to treat cytokine storm seen in COVID-19, immune check point inhibitory (ICI) therapy, sepsis and ARDS (acute respiratory disease). This is further supported by the observation that GLA, DGLA and AA inactivate enveloped viruses including COVID-19. Thus, infusions of appropriate amounts of GLA, DGLA, AA, PGE2 and LXA4 are of significant therapeutic benefit in COVID-19, ICI therapy and other inflammatory conditions including but not limited to sepsis. AA is the precursor of both PGE2 and LXA4 suggesting that AA is most suited for such preventive and therapeutic approach.

[9] *Brailovski E, Kim RB, Juurlink D*. **Rosuvastatin Myotoxicity After Starting Canagliflozin Treatment: A Case Report**. Annals of internal medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32744865
ABSTRACT

[10] *Sugizaki Y, Otake H, Kuroda K et al.* **Concomitant Use of Rosuvastatin and Eicosapentaenoic Acid Significantly Prevents Native Coronary Atherosclerotic Progression in Patients With In-Stent Neoatherosclerosis**. Circulation journal : official journal of the Japanese Circulation Society 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759543

ABSTRACT

BACKGROUND: In-stent neoatherosclerosis (NA) is a risk for future cardiovascular events through atherosclerotic progression in non-stented lesions. Using optical coherence tomography, this study assessed the efficacy of intensive therapy with 10 mg/day rosuvastatin plus 1,800 mg/day eicosapentaenoic acid (EPA) vs. standard 2.5 mg/day rosuvastatin therapy on native coronary plaques in patients with NA.Methods and Results:This was a subgroup analysis of the randomized LINK-IT trial, which was designed to compare changes in the lipid index in NA between intensive and standard therapy for 12 months. In all, 42 patients with native coronary plaques and NA were assessed. Compared with standard therapy, intensive therapy resulted in greater decreases in serum low-density lipoprotein cholesterol concentrations and greater increases in serum 18-hydroxyeicosapentaenoic acid concentrations, with significantly greater decreases in the lipid index and macrophage grade in both NA (-24 vs. 217 [P<0.001] and -15 vs. 24 [P<0.001], respectively) and native coronary plaques (-112 vs. 29 [P<0.001] and -17 vs. 1 [P<0.001], respectively) following intensive therapy. Although there was a greater increase in the macrophage grade in NA than in native coronary plaques in the standard therapy group, in the intensive therapy group there were comparable reductions in macrophage grade between NA and native coronary plaques. CONCLUSIONS: Compared with standard therapy, intensive therapy prevented atherosclerotic progression more effectively in native coronary plaques in patients with NA.

[11] *Rizo-Liendo A, Sifaoui I, Arberas-Jiménez I et al.* **Fluvastatin and atorvastatin induce programmed cell death in the brain eating amoeba Naegleria fowleri**. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2020; 130:110583.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32745907

ABSTRACT

Naegleria fowleri is the causative agent of a type of encephalitis called Primary Amoebic Encephalitis (PAM). Almost 98 % of PAM cases reported worldwide are fatal and affect mostly immunocompetent children and young adults. The current therapeutic option against PAM cases includes a combination of miltefosine, amphotericin B and other drugs which are unfortunately associated with severe side effects. In a recent study in our group, statins were tested in vitro against Naegleria fowleri trophozoites showing activity against these pathogens at low concentrations causing low toxicity. Consequently, there is an urgent need to develop novel PAM therapeutic options. Therefore, this study was undertaken to evaluate the pathway of cell death induced by two of the previously tested molecules, fluvastatin and atorvastatin. Moreover, these statins were compared to miltefosine and amphotericin B. Furthermore, the induction of Programmed Cell Death (PCD) instead of necrosis in treated amoebae would be the ideal situation since necrosis could lead to non-desired inflammation processes in the infected individual. The obtained results revealed that both statins induced PCD in the treated amoebae after the observation of condensed chromatin, cell membrane damages, mitochondrial membrane potential and ATP levels collapse and ROS generation. In conclusion, both fluvastatin and atorvastatin could be potential new candidates for PAM therapy since they are active at low concentrations, induce low toxicity and cause PCD in the treated amoebae, hence avoiding the activation of inflammation pathways.

[12] *Orces CH, Montalvan M, Tettamanti D*. **The Effect of Statins on Serum Vitamin D Concentrations Among Older Adults**. Cureus 2020; 12:e8950.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32765995
ABSTRACT
Background Randomized and observational studies have previously reported inconsistent results for the direct association between statin therapy and 25, hydroxyvitamin D [25(OH)D] levels. Thus, the present study aimed to examine the relationship between statin use and 25(OH)D and its metabolites concentrations in a large nationally representative sample of older adults. Methods This study was conducted using data from the National Health and Nutrition Examination Survey. Participants were asked to show the medication containers of all the products used in the previous 30 days, and the prescription of statins was defined on the three-level nested therapeutic classification scheme of Cerner Multum's Lexicon. General linear models adjusted for potential confounders were created to compare 25(OH)D concentrations between older adults taking statins and those who did not. Results A total of 6,261 participants with a mean age of 69.5 years comprised the study sample. Of those, 40.2% were taking statins with a median length of therapy of 5 years. Adjusted mean 25(OH)D(3) and 25(OH)D levels were 3.3 and 4.4 nmol/L higher among participants taking statins than those who did not, respectively. Moreover, this association was consistently seen regardless of the duration of therapy and particularly in subjects taking simvastatin, atorvastatin, or rosuvastatin. In subgroup analyses according to BMI categories and vitamin D intake, higher 25(OH)D levels were also seen among statin users. By contrast, this association was attenuated among those with a daily vitamin D between 400 and 800 and >800 IU. Conclusion Older adults on statin therapy had significantly higher serum 25(OH)D concentrations. Additional research should be conducted to define the mechanism of this association and determine if the pleiotropic effects attributed to statins may be mediated by vitamin D.

[13] *Montvida O, Verma S, Shaw JE, Paul SK*. **Cardiometabolic Risk Factor Control in African American and White Caucasians initiating SGLT-2 Inhibitor: Real-world Study**. Diabetes Obes Metab 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32744394
ABSTRACT
AIMS: To explore cardiometabolic risk profiles, probability of sustainable control, and the effectiveness of treatment with SGLT-2i in African American (AA) and White Caucasian (WC). MATERIALS AND METHODS: Using nationally representative US electronic medical records, 72 690 WC and 10 004 AA adults diagnosed with type 2 diabetes initiating SGLT-2i during 2013-2018, continuing it ≥6 months, and with follow-up ≥12 months, were identified. HbA1c, body weight, SBP, and lipid changes at 6-month and sustainability of control over 18 months post SGLT-2i initiation were explored, separately in those with and without atherosclerotic cardiovascular disease (ASCVD). RESULTS: WC were older (58 years) with lower mean HbA1c (8.5%), compared to AA (54 years, HbA1c 9.0%). BMI distribution was similar, proportions of uncontrolled SBP /LDL-C /non-HDL-C/ Triglyceride were 24/ 42 /51 /62% in WC and 31/ 51 /49 / 32% in AA. At 6-month follow-up WC and AA had similar adjusted reduction in HbA1c (1.1%), SBP (8-10 mmHg), LDL-C (10-13 mg/dL) and body weight (1.1-1.4 kg). However, over 18 months follow-up, compared to WC, AA were significantly less likely to achieve a sustainable control in HbA1c (OR: 0.67; 95% CI: 0.63-0.72), body weight (OR: 0.81;

95% CI: 0.72-0.91), SBP (OR: 0.67; 95% CI: 0.61-0.74), LDL-C (OR: 0.77; 95% CI: 0.67-0.89). Triglyceride control was significantly better among AA. AA had significantly higher risk factor burden irrespective of ASCVD status. CONCLUSIONS: While effectiveness of SGLT-2i was similar among AA and WC irrespective of ASCVD status, AA continued to have worse cardiometabolic risk factor burden post SGLT-2i initiation.

[14] *Kornholt J, Christensen MB*. **Prevalence of polypharmacy in Denmark**. Danish medical journal 2020; 67.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32741431
ABSTRACT
INTRODUCTION: Polypharmacy is associated with an increased risk of adverse health outcomes. This study aims to describe the prevalence of polypharmacy and medication use among older Danish citizens. METHODS: From national registers, we extracted medicine use in relation to age group and residential region for the entire Danish population for the first half of 2016. The most frequently redeemed medicines among older citizens (≥ 75 years) in 2016 were grouped into clinically meaningful medication classes. RESULTS: The prevalence of polypharmacy (> 5 different medicines) was 51% among citizens ≥ 75 years compared with 12% for the entire Danish population. The prevalence of polypharmacy increased with age and was 7% among citizens aged 40-49 years compared with 66% among citizens aged ≥ 90 years. There were only minor regional differences in the prevalence of polypharmacy. The most commonly redeemed medicine classes and individual medicines for older citizens were: 1) pain medication: paracetamol (50%) and tramadol (14%); 2) cardiovascular medicines: acetylsalicylic acid (26%), simvastatin (25%), metoprolol (22%), amlodipine (21%), furosemide (20%), bendroflumethiazide (17%), and losartan (14%); and 3) gastrointestinal medicines: pantoprazole (15%). CONCLUSIONS: Polypharmacy is prevalent in Denmark with no relevant regional differences. The prevalence of polypharmacy increased with age, and more than half of the population aged ≥ 75 years redeemed prescriptions for > 5 different medicines. The most redeemed medicines among older citizens were against pain and cardiovascular disease. FUNDING: none. TRIAL REGISTRATION: not relevant.

[15] *G ZP, Kochiadakis G, Lazopoulos G et al.* **Targeting vulnerable atherosclerotic plaque via PET-tracers aiming at cell-surface overexpression of somatostatin receptors**. Biomedical reports 2020; 13:9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32765848
ABSTRACT
Cardiovascular disease (CD) is the leading cause of death in the developed world, with major atherothrombotic events, being mainly attributed to the rupture of unstable, vulnerable atherosclerotic lesions, leading to blood flow obstruction. Since unstable atherosclerotic plaques frequently do not cause hemodynamically significant blood flow restriction, conventional stress imaging tests cannot depict the vulnerable, high-risk for rupture atherosclerotic lesions. Therefore, molecular imaging techniques targeting specific pathophysiologic features related to atherosclerotic plaque rupture mechanism, hold promise for precise and individualized treatment strategies of CD. In the current report, we describe in a patient diagnosed with pancreatic neuroendocrine tumor, the selective uptake of (68)Ga-DOATATE by an atherosclerotic lesion in the thoracic aorta. This data indicates that (68)Ga-

DOTATATE, which is a positron emitting tomography tracer, targeting the recruitment of macrophages taking place in the vulnerable plaque, could potentially serve as an imaging probe for the detection of high-risk, prone to rupture plaques.

[16] *Ferguson K, Quail N, Kewin P, Blyth KG*. **COVID-19 associated with extensive pulmonary arterial, intracardiac and peripheral arterial thrombosis**. BMJ case reports 2020; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32747597
ABSTRACT
We describe a patient with COVID-19 who developed simultaneous pulmonary, intracardiac and peripheral arterial thrombosis. A 58-year-old man, without major comorbidity, was admitted with a 14-day history of breathlessness. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection was confirmed by laboratory testing. Initial imaging revealed COVID-19 pneumonia but no pulmonary thromboembolism (PTE) on CT pulmonary angiography (CTPA). The patient subsequently developed respiratory failure and left foot ischaemia associated with a rising D-dimer. Repeat CTPA and lower limb CT angiography revealed simultaneous bilateral PTE, biventricular cardiac thrombi and bilateral lower limb arterial occlusions. This case highlights a broad range of vascular sequalae associated with COVID-19 and the fact that these can occur despite a combination of prophylactic and treatment dose anticoagulation.

[17] *Chu CS, Law SH, Lenzen D et al.* **Clinical Significance of Electronegative Low-Density Lipoprotein Cholesterol in Atherothrombosis**. Biomedicines 2020; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32751498
ABSTRACT
Despite the numerous risk factors for atherosclerotic cardiovascular diseases (ASCVD), cumulative evidence shows that electronegative low-density lipoprotein (L5 LDL) cholesterol is a promising biomarker. Its toxicity may contribute to atherothrombotic events. Notably, plasma L5 LDL levels positively correlate with the increasing severity of cardiovascular diseases. In contrast, traditional markers such as LDL-cholesterol and triglyceride are the therapeutic goals in secondary prevention for ASCVD, but that is controversial in primary prevention for patients with low risk. In this review, we point out the clinical significance and pathophysiological mechanisms of L5 LDL, and the clinical applications of L5 LDL levels in ASCVD can be confidently addressed. Based on the previously defined cut-off value by receiver operating characteristic curve, the acceptable physiological range of L5 concentration is proposed to be below 1.7 mg/dL. When L5 LDL level surpass this threshold, clinically relevant ASCVD might be present, and further exams such as carotid intima-media thickness, pulse wave velocity, exercise stress test, or multidetector computed tomography are required. Notably, the ultimate goal of L5 LDL concentration is lower than 1.7 mg/dL. Instead, with L5 LDL greater than 1.7 mg/dL, lipid-lowering treatment may be required, including statin, ezetimibe or PCSK9 inhibitor, regardless of the low-density lipoprotein cholesterol (LDL-C) level. Since L5 LDL could be a promising biomarker, we propose that a high throughput, clinically feasible methodology is urgently required not only for conducting a prospective, large population study but for developing therapeutics strategies to decrease L5 LDL in the blood.

[18] *Baul PB, Deepak AD, Kakkar M, Modi S*. **Effect of Atorvastatin on blood ketone levels and glycemic control in patients with type 2 diabetes mellitus: A single arm pilot study**. Diabetes & metabolic syndrome 2020; 14:1333-1337.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32755832

ABSTRACT

BACKGROUND AND AIMS: Cholesterol and ketone bodies are synthesized in liver from a common precursor acetyl coenzyme A (acetyl-CoA). Statins by inhibiting cholesterol synthesis may lead to accumulation of acetyl-CoA in hepatocytes and its diversion towards ketogenesis. Ketone bodies may act as alternative energy source thus sparing blood glucose and contributing to hyperglycemia. The present study aims to assess the effect of Atorvastatin therapy on blood ketone levels and glycemic control in patients with T2DM. METHODS: Study included 24 statin naïve subjects with T2DM. They were prescribed tablet Atorvastatin at dose of 10 mg once daily at bedtime. Ongoing anti-diabetic medications were not changed. Estimation of blood ketones, urine ketones, fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), glycated hemoglobin (HbA1c) and lipid parameters was carried out at baseline and at 3 months after starting Atorvastatin. RESULTS: There was moderate but significant increase in blood ketones (0.16 ± 0.08 mmol/L vs. 0.26 ± 0.07 mmol/L; p-value = 0.0000), FPG (133.8 ± 17.91 mg/dL vs. 143.3 ± 22.99 mg/dL; p-value = 0.0016) and PPG (193.0 ± 36.54 mg/dL vs. 211.0 ± 49.51 mg/dL; p-value = 0.0344) after 3 months of Atorvastatin therapy. This was associated with significant reduction in serum total cholesterol and low density lipoprotein cholesterol. CONCLUSION: Three months therapy with Atorvastatin at the dose of 10 mg once daily at bedtime in patients with T2DM resulted in moderate rise in blood ketone levels, FPG and PPG in addition to improvement in lipid parameters.

[19] *Adashek JJ, Redding D*. **A Pilot Study on the Effects of Nut Consumption on Cardiovascular Biomarkers**. Cureus 2020; 12:e8798.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32742827

ABSTRACT

BACKGROUND: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in the United States and changes in lifestyle can minimize the likelihood of succumbing to heart disease. Anti-inflammatory agents are commonly used to reduce the chronic inflammatory state behind the pathogenesis of CVD. Multiple studies have been published correlating nut consumption with a reduction in both heart attacks and strokes. The goal of this study is to determine to what extent the consumption of almonds, hazelnuts, and walnuts have on the blood markers associated with cardiac disease and inflammation. METHODS: This was a six-week study in which subject's baseline values act as controls. Fasting blood draws occurred at week 0, week 2, and after four weeks of intervention (week 6). All participants had undesirable lipid profiles and no medications related to heart disease. RESULTS: Total cholesterol (TC): high-density lipoprotein (HDL-C) ratio was lowered a statistically significant amount at the six-week time point (3.89 ± 0.74) compared to both the zero-week (4.93 ± 1.16, $p < 0.01$) and two-week (4.63 ± 1.20, $p < 0.5$) timepoints. Low-density lipoprotein (LDL) measurements were lowered a statistically significant amount at the six-week time point (135.6 ± 15.0 mg/dL) compared to the zero-week (159.7 ± 12.3 mg/dL, $p < 0.01$). Erythrocyte sedimentation rate (ESR) was lowered a statistically significant amount at six-week time point (10.44 ± 5.05 mm/h) compared to the zero-week (14.44 ± 5.12 mm/h, $p < 0.01$). CONCLUSIONS: Blood

markers associated with CVD specifically and the general marker for inflammation associated with many chronic diseases can be favorably modified with the consumption of specific nuts as demonstrated by this study.

[20] *Steinkohl F, Barbieri F, Senoner T et al.* **Coronary atherosclerosis profile in patients with end-stage liver disease prior to liver transplantation due to alcoholic fatty liver: a coronary CTA study**. European radiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32749590
ABSTRACT
OBJECTIVES: To assess the coronary atherosclerosis profile by coronary computed tomography angiography (CTA) in patients with end-stage liver disease (ESLD) due to alcohol-related liver disease (ARLD) evaluated for liver transplantation (LT), in a retrospective matched case-controlled cohort study. METHODS: One hundred forty patients (age 60.6 years ± 9.8, 20.7% females) who underwent coronary CTA were included. Seventy patients with ESLD due to ARLD (ESLD-alc) were propensity score (1:1) matched for age, gender, and the major 5 cardiovascular risk factors with healthy controls. CTA analysis included the following: stenosis severity according to CAD-RADS as (0) = no, (1) minimal < 25%, (2) mild 25-50%, (3) moderate 50-70%, and (4) severe > 70% stenosis, total mixed plaque burden weighted for non-calcified component (G-score) and high-risk plaque criteria (Napkin-Ring, low attenuation plaque, spotty calcification, positive remodeling). RESULTS: Prevalence of coronary artery disease (CAD) was high (84.4%) in the ESLD-alc group but similar to controls. Stenosis severity was similar (CAD-RADS, 1.9 vs. 2.2, p = 0.289). High-grade stenosis (> 70%) was observed in 12.5% of ESLD-alc patients. High-risk plaques were less frequent in the ESLD-alc cohort as compared to controls (4.5% vs. 37.5%, p < 0.001), and total mixed plaque burden was lower (G-score, 4.9 versus 7.4, p = 0.001). Plaque density was lower in controls (56.6HU ± 3.2 vs. 91.3HU ± 4.5, p = 0.007) indicating more lipid-rich in controls, but higher mixed fibro-calcific plaque component in those with alcohol-related ESLD. CONCLUSION: Patients with alcohol-related ESLD exhibit more mixed fibro-calcified plaques but less plaque with high-risk features and less fibro-fatty plaque burden, while total CAD prevalence is high. KEY POINTS: • Patients with ESLD prior to LT have a high total prevalence of CAD and stenosis severity, which is similar to those of healthy controls with an identical cardiovascular risk profile. • Patients with ESLD prior to LT due to alcohol abuse have more calcific but less fibro-fatty plaque and less high-risk plaque. • CTA seems to be a useful imaging technique for risk stratification prior to LT.

[21] *Perrot N, Valerio V, Moschetta D et al.* **Genetic and In Vitro Inhibition of PCSK9 and Calcific Aortic Valve Stenosis**. JACC. Basic to translational science 2020; 5:649-661.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32760854
ABSTRACT
The authors investigated whether PCSK9 inhibition could represent a therapeutic strategy in calcific aortic valve stenosis (CAVS). A meta-analysis of 10 studies was performed to determine the impact of the PCSK9 R46L variant on CAVS, and the authors found that CAVS was less prevalent in carriers of this variant (odds ratio: 0.80 [95% confidence interval: 0.70 to 0.91]; p = 0.0011) compared with noncarriers. PCSK9 expression was higher in the aortic valves of patients CAVS compared with control patients. In human valve interstitials cells

submitted to a pro-osteogenic medium, PCSK9 levels increased and a PCSK9 neutralizing antibody significantly reduced calcium accumulation.

[22] *Majdalawieh AF, Dalibalta S, Yousef SM*. **Effects of sesamin on fatty acid and cholesterol metabolism, macrophage cholesterol homeostasis and serum lipid profile: A comprehensive review**. European journal of pharmacology 2020; 885:173417.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32750369
ABSTRACT
Sesamin is the major lignan constituent derived from Sesamum indicum seeds and sesame oil. Various studies have reported that sesamin possesses potent lipid-lowering properties. The lipid-lowering effects of sesamin have been mainly attributed to its ability in affecting key events in fatty acid and cholesterol metabolism and in lowering atherogenesis-triggering LDL, VLDL and TG levels, as well as in increasing atheroprotective HDL levels. In this review, we provide a comprehensive summary of the reported anti-hyperlipidemic effects of sesamin, presented both in vitro and in vivo. The molecular anti-hyperlipidemic properties of sesamin that underlie its well-documented anti-atherogenic effects are thoroughly discussed and analyzed. Studies focusing on the ability of sesamin to inhibit fatty acid synthesis, induce fatty acid oxidation, inhibit cholesterol synthesis and absorption and maintain macrophage cholesterol homeostasis are outlined. The effects of sesamin on circulating serum and liver lipid levels are also highlighted. Moreover, the anti-hyperlipidemic effects of sesamin are compared to those of other important sesame lignans like sesamolin and episesamin. Findings reveal that sesamin mainly exerts its anti-hyperlipidemic effects by targeting Δ5 desaturase, HMGCR, ABCA1 and ABCG1 through PPARα, PPARγ, LXRα, and SREBP signaling pathways. Overall, the amount of evidence supporting the anti-hyperlipidemic potential of sesamin in vitro and in vivo is compelling. A thorough understanding of the mechanisms underlying the anti-hyperlipidemic properties of sesamin is imperative for the possible employment of sesamin as an anti-hyperlipidemic and anti-atherogenic agent with minimal side effects.

[23] *Li W, Ren X, Zhang L*. **Clinical efficacy of atorvastatin calcium combined with aspirin in patients with acute ischemic stroke and effect on neutrophils, lymphocytes and IL-33**. Experimental and therapeutic medicine 2020; 20:1277-1284.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32765667
ABSTRACT
Clinical efficacy of atorvastatin calcium combined with aspirin in patients with acute ischemic stroke (AIS) and its effect on neutrophils to lymphocytes ratio (NLR) and interleukin-33 (IL-33) were investigated. In total, 108 patients with AIS in Luoyang Central Hospital Affiliated to Zhengzhou University from April 2016 to October 2017 were selected. There were 56 cases treated with atorvastatin calcium combined with aspirin as the observation group, and 52 cases were treated with aspirin alone as the control group. The clinical effect was observed. The NLR and IL-33 levels were measured by routine blood test and enzyme linked immunosorbent assay (ELISA) before and after treatment. The scores of the National Institutes of Health Stroke scale (NIHSS) and the occurrence of complications were collected before and after treatment in the two groups. Modified Rankin Scale (MRS) was used to evaluate the curative effect. Score ≤2 points is effective in the treatment. Pearson's analysis was used to analyze the correlation between NLR, IL-33 and NIHSS score. The total hospitalization time and 1 year

survival rate were compared. The total effective rate of treatment in the observation group was higher than that in the control group (P<0.05). There was no difference in NLR and IL-33 levels between the two groups before treatment (P>0.05). After treatment, the NLR in the observation group was significantly lower than that in the control group (P<0.05). After treatment, the NIHSS score, the total number of complications and the total hospitalization time in the observation group were significantly lower than those in the control group (P<0.05). Pearson's analysis showed a positive correlation between NLR and NIHSS score (r=0.681, P<0.001), and a negative correlation between IL-33 and NIHSS score (r=-0.708, P<0.001). In conclusion, atorvastatin calcium combined with aspirin has a better effective rate in the treatment of acute ischemic stroke than aspirin alone. The combination can better reduce the NLR, increase the expression level of IL-33 in serum, reduce the occurrence of complications and hospitalization time, and increase the survival rate of patients.

[24] *Junaid A, Schoeman J, Yang W et al.* **Metabolic response of blood vessels to TNFα**. eLife 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32749215
ABSTRACT
TNFα signaling in the vascular endothelium elicits multiple inflammatory responses that drive vascular destabilization and leakage. Bioactive lipids are main drivers of these processes. In vitro mechanistic studies of bioactive lipids have been largely based on two-dimensional endothelial cell cultures that, due to lack of laminar flow and the growth of the cells on non-compliant stiff substrates, often display a pro-inflammatory phenotype. This complicates the assessment of inflammatory processes. Three-dimensional microvessels-on-a-chip models provide a unique opportunity to generate endothelial microvessels in a more physiological environment. Using an optimized targeted liquid chromatography-tandem mass spectrometry measurements of a panel of pro- and anti-inflammatory bioactive lipids, we measure the profile changes upon administration of TNFα. We demonstrate that bioactive lipid profiles can be readily detected from three-dimensional microvessels-on-a-chip and display a more dynamic, less inflammatory response to TNFα, that resembles more the human situation, compared to classical two-dimensional endothelial cell cultures.
In a range of conditions called autoimmune diseases, the immune system attacks the body rather than foreign elements. This can cause inflammation that is harmful for many organs. In particular, immune cells can produce excessive amounts of a chemical messenger called tumor necrosis factor alpha (TNFα for short), which can lead to the release of fatty molecules that damage blood vessels. This process is normally studied in blood vessels cells that are grown on a dish, without any blood movement. However, in this rigid 2D environment, the cells become ‘stressed’ and show higher levels of inflammation than in the body. This makes it difficult to assess the exact role that TNFα plays in disease. A new technology is addressing this issue by enabling scientist to culture blood vessels cells in dishes coated with gelatin. This allows the cells to organize themselves in 3D, creating tiny blood vessels in which fluids can flow. However, it was unclear whether these ‘microvessels-on-a-chip’ were better models to study the role of TNFα compared to cells grown on a plate. Here, Junaid et al. compared the levels of inflammation in blood vessels cells grown in the two environments, showing that cells are less inflamed when they are cultured in 3D. In addition, when the artificial 3D-blood vessels were exposed to TNFα, they responded more like real blood vessels than the 2D models. Finally, experiments showed that it was possible to monitor the release of fatty molecules in

this environment. Together, this work suggests that microvessels-on-a-chip are better models to study how TNFα harms blood vessels. Next, systems and protocols could be develop to allow automated mass drug testing in microvessels-on-a-chip. This would help scientists to quickly screen thousands of drugs and find candidates that can protect blood vessels from TNFα.
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[25] *German CA, Shapiro MD*. **Assessing Atherosclerotic Cardiovascular Disease Risk with Advanced Lipid Testing: State of the Science**. European cardiology 2020; 15:e56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32742310
ABSTRACT
Cardiovascular disease is the number one cause of death and disability worldwide. While substantial gains have been made in reducing cardiovascular mortality, future projections suggest that we have reached a nadir and may be at an inflection point, given the rising tide of obesity and diabetes. Evaluation and management of plasma lipids is central to the prevention of atherosclerotic cardiovascular disease. Although the standard lipid panel represents a well-established platform to assess risk, this test alone can be insufficient and/or misleading. Advances in our understanding of atherosclerosis have led to the development of lipid-based biomarkers that help to discriminate the risk of cardiovascular disease when it is unclear. While these biomarkers provide novel information, their implementation into clinical medicine remains difficult given discrepancies in the literature, lack of assay standardisation, poor accessibility and high cost. However, additional measures of atherogenic lipoproteins or their surrogates may offer insight beyond the standard lipid panel, providing a more precise assessment of risk and more accurate assessment of lipid-lowering therapy.

[26] *Esan O, Wierzbicki AS*. **Volanesorsen in the Treatment of Familial Chylomicronemia Syndrome or Hypertriglyceridaemia: Design, Development and Place in Therapy**. Drug design, development and therapy 2020; 14:2623-2636.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32753844
ABSTRACT
Severe hypertriglyceridaemia is associated with pancreatitis and chronic pancreatitis-induced diabetes. Familial chylomicronaemia syndrome (FCS) is a rare autosomal recessive disorder of lipid metabolism characterised by high levels of triglycerides (TGs) due to failure of chylomicron clearance. It causes repeated episodes of severe abdominal pain, fatigue and attacks of acute pancreatitis. There are few current options for its long-term management. The only universal long-term therapy is restriction of total dietary fat intake to <10-15% of daily calories (15 to 20g per day). Many patients have been treated with fibrates and statins with a variable response, but many remain susceptible to pancreatitis. Other genetic syndromes associated with hypertriglyceridaemia include familial partial lipodystrophy (FPLD). Targeting apolipoprotein C3 (apoC3) offers the ability to increase clearance of chylomicrons and other triglyceride-rich lipoproteins. Volanesorsen is an antisense oligonucleotide (ASO) inhibitor of apoC3, which reduces TG levels by 70-80% which has been shown also to reduce rates of pancreatitis and improve well-being in FCS and reduce TGs and improve insulin resistance in FPLD. It is now undergoing licensing and payer reviews. Further developments of antisense technology including small interfering RNA therapy to apoC3 as well as other approaches to modulating triglycerides are in development for this rare disorder.

[27] *Eriksen R, Perez IG, Posma JM et al.* **Dietary metabolite profiling brings new insight into the relationship between nutrition and metabolic risk: An IMI DIRECT study**. EBioMedicine 2020; 58:102932.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32763829
ABSTRACT
BACKGROUND: Dietary advice remains the cornerstone of prevention and management of type 2 diabetes (T2D). However, understanding the efficacy of dietary interventions is confounded by the challenges inherent in assessing free living diet. Here we profiled dietary metabolites to investigate glycaemic deterioration and cardiometabolic risk in people at risk of or living with T2D. METHODS: We analysed data from plasma collected at baseline and 18-month follow-up in individuals from the Innovative Medicines Initiative (IMI) Diabetes Research on Patient Stratification (DIRECT) cohort 1 n = 403 individuals with normal or impaired glucose regulation (prediabetic) and cohort 2 n = 458 individuals with new onset of T2D. A dietary metabolite profile model (T(pred)) was constructed using multivariable regression of 113 plasma metabolites obtained from targeted metabolomics assays. The continuous T(pred) score was used to explore the relationships between diet, glycaemic deterioration and cardio-metabolic risk via multiple linear regression models. FINDINGS: A higher T(pred) score was associated with healthier diets high in wholegrain (β=3.36 g, 95% CI 0.31, 6.40 and β=2.82 g, 95% CI 0.06, 5.57) and lower energy intake (β=-75.53 kcal, 95% CI -144.71, -2.35 and β=-122.51 kcal, 95% CI -186.56, -38.46), and saturated fat (β=-0.92 g, 95% CI -1.56, -0.28 and β=-0.98 g, 95% CI -1.53, -0.42 g), respectively for cohort 1 and 2. In both cohorts a higher T(pred) score was also associated with lower total body adiposity and favourable lipid profiles HDL-cholesterol (β=0.07 mmol/L, 95% CI 0.03, 0.1), (β=0.08 mmol/L, 95% CI 0.04, 0.1), and triglycerides (β=-0.1 mmol/L, 95% CI -0.2, -0.03), (β=-0.2 mmol/L, 95% CI -0.3, -0.09), respectively for cohort 1 and 2. In cohort 2, the T(pred) score was negatively associated with liver fat (β=-0.74%, 95% CI -0.67, -0.81), and lower fasting concentrations of HbA1c (β=-0.9 mmol/mol, 95% CI -1.5, -0.1), glucose (β=-0.2 mmol/L, 95% CI -0.4, -0.05) and insulin (β=-11.0 pmol/mol, 95% CI -19.5, -2.6). Longitudinal analysis showed at 18-month follow up a higher T(pred) score was also associated lower total body adiposity in both cohorts and lower fasting glucose (β=-0.2 mmol/L, 95% CI -0.3, -0.01) and insulin (β=-9.2 pmol/mol, 95% CI -17.9, -0.4) concentrations in cohort 2. INTERPRETATION: Plasma dietary metabolite profiling provides objective measures of diet intake, showing a relationship to glycaemic deterioration and cardiometabolic health. FUNDING: This work was supported by the Innovative Medicines Initiative Joint Undertaking under grant agreement no. 115,317 (DIRECT), resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies.

[28] *Doggrell SA*. **Inclisiran, the billion-dollar drug, to lower LDL cholesterol - is it worth it?** Expert opinion on pharmacotherapy 2020:1-4.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32749892
ABSTRACT
INTRODUCTION: If statins are unsuccessful at achieving the LDL cholesterol level goal in subjects with hypercholesterolemia, non-statin therapy should be added to reduce cardiovascular morbidity and mortality. The first inhibitors of proprotein convertase substilisin-kexin type 9 (PCSK9) were human monoclonal antibodies and these reduced LDL cholesterol

and cardiovascular events. Inclisiran is a small interfering RNA molecule (siRNAs) directed against PCSK9. AREAS COVERED: This key paper evaluation focuses on Phase 3 trials that assess inclisiran in the treatment of hypercholesterolemia and heterozygous familial hypercholesterolemia. EXPERT OPINION: To date, the findings with inclisiran have been very promising as it causes large decreases in LDL cholesterol with few adverse effects. However, there are some limitations to its widespread use. Firstly, cardiovascular outcomes trials have not been completed, so we do not know how inclisiran compares to the PCSK9 monoclonal antibodies, which, seem to me, to only have a modest effect on cardiovascular outcomes. Secondly, a major problem with the PCSK9 monoclonal antibodies is that they are expensive, and their use is often discontinued or not pursued, which can leave the subjects intended for treatment at high cardiovascular risk. At present, it is not clear whether similar problems around cost will apply to inclisiran.

[29] *Dahik VD, Frisdal E, Le Goff W*. **Rewiring of Lipid Metabolism in Adipose Tissue Macrophages in Obesity: Impact on Insulin Resistance and Type 2 Diabetes**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32752107
ABSTRACT
Obesity and its two major comorbidities, insulin resistance and type 2 diabetes, represent worldwide health issues whose incidence is predicted to steadily rise in the coming years. Obesity is characterized by an accumulation of fat in metabolic tissues resulting in chronic inflammation. It is now largely accepted that adipose tissue inflammation underlies the etiology of these disorders. Adipose tissue macrophages (ATMs) represent the most enriched immune fraction in hypertrophic, chronically inflamed adipose tissue, and these cells play a key role in diet-induced type 2 diabetes and insulin resistance. ATMs are triggered by the continuous influx of dietary lipids, among other stimuli; however, how these lipids metabolically activate ATM depends on their nature, composition and localization. This review will discuss the fate and molecular programs elicited within obese ATMs by both exogenous and endogenous lipids, as they mediate the inflammatory response and promote or hamper the development of obesity-associated insulin resistance and type 2 diabetes.

[30] *Cui L, Zhou W, Xi B et al.* **Increased risk of metabolic dysfunction in children conceived by assisted reproductive technology**. Diabetologia 2020; 63:2150-2157.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32757153
ABSTRACT
AIMS/HYPOTHESIS: Assisted reproductive technology (ART) is the most widely used treatment for infertility and has resulted in millions of births worldwide. The safety of the offspring has been of the utmost concern. Previous studies suggested an increase in metabolic disorders in offspring later in life. The aim of the present study was to investigate metabolic changes at age 6-10 years in offspring conceived as a result of in vitro fertilisation/intracytoplasmic sperm injection (IVF/ICSI). METHODS: A total of 380 children born from IVF/ICSI and a matched control group of 380 naturally conceived children, all aged 6-10 years, were recruited. Anthropometric measures, ultrasound and serum tests were performed for body mass, glucose metabolism and lipid profiles, and examination of vasculature structure. RESULTS: The children conceived by ART showed significantly higher fasting blood glucose and serum insulin levels and HOMA-IR (adjusted β [95% CI]: fasting

blood glucose 0.49 [0.42, 0.55]; log(e)-transformed insulin 0.28 [0.20, 0.35]; log(e)-transformed HOMA-IR 0.38 [0.30, 0.46]), as well as a lower HOMA-B and serum apolipoprotein A (ApoA) levels (adjusted β [95% CI]: log(e)-transformed HOMA-B -0.19 [-0.27, -0.11]; ApoA -0.17 [-0.21, -0.13]), when compared with the control group. Furthermore, the ultrasound scan indicated elevated carotid intima-media thickness in children conceived by ART (β 0.13 [95% CI 0.12, 0.13]). CONCLUSIONS/INTERPRETATION: Children conceived by IVF/ICSI have a less favourable glucose and cardiovascular metabolic profile in childhood when compared with naturally conceived children. The underlying mechanisms and potential long-term consequences need to be elucidated in future studies. Graphical abstract.

[31] *Wang H, Yang H, Liu Z et al.* **Targeted Genetic Analysis in a Chinese Cohort of 208 Patients Related to Familial Hypercholesterolemia**. Journal of atherosclerosis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759540
ABSTRACT
AIM: Familial hypercholesterolemia (FH) is the most commonly encountered genetic condition that predisposes individuals to severe autosomal dominant lipid metabolism dysfunction. Although more than 75% of the European population has been scrutinized for FH-causing mutations, the genetic diagnosis proportion among Chinese people remains very low (less than 0.5%). The aim of this study was to identify genetic mutations and help make a precise diagnosis in Chinese FH patients. METHODS: We designed a gene panel containing 20 genes responsible for FH and tested 208 unrelated Chinese possible/probable or definite FH probands. In addition, we called LDLR copy number variation (CNVs) with the panel data by panelcn.MOPS, and multiple ligation-dependent probe amplification (MLPA) was used to search for CNVs in LDLR, APOB, and PCSK9. RESULTS: A total of 79 probands (38.0%) tested positive for a (likely) pathogenic mutation, most of which were LDLR mutations, and three LDLR CNVs called from the panel data were all successfully confirmed by MLPA analysis. In total, 48 different mutations were identified, including 45 LDLR mutations, 1 APOB mutation, 1 ABCG5 mutation, and 1 APOE mutation. Among them, the five most frequent mutations (LDLR c.1879G＞A, c.1747C＞T, c.313＋1G＞A, c.400T＞C, and APOB c.10579C ＞T) were detected. Moreover, we also found that patients with LDLR variants of CNVs and splicing and nonsense had increased low-density lipoprotein cholesterol levels when compared with those who carried missense variants. CONCLUSIONS: The spectrum of FH-causing mutations in the Chinese population is refined and expanded. Analyses of FH causal genes have been a great help in clinical diagnosis and have deep implications in disease treatment. These data can serve as a considerable dataset for next-generation sequencing analysis of the Chinese population with FH and contribute to the genetic diagnosis and counseling of FH patients.

[32] *Silverio A, Benvenga RM, Piscione F et al.* **Prevalence and Predictors of Out-of-Target LDL Cholesterol 1 to 3 Years After Myocardial Infarction. A Subanalysis From the EYESHOT Post-MI Registry**. Journal of cardiovascular pharmacology and therapeutics 2020:1074248420947633.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32757779
ABSTRACT

BACKGROUND: There is an incomplete understanding of the prevalence and predictors of attainment of low-density lipoprotein cholesterol (LDL-C) goal after myocardial infarction (MI). AIM: To evaluate the prevalence of achievement of LDL-C goal of 70 mg/dL, to identify the baseline features associated with suboptimal lipid control, and to assess the use of LDL-C-lowering drug therapies (LLT) beyond the first year after MI. METHODS: The EYESHOT Post-MI was a prospective, cross-sectional, Italian registry, which enrolled patients presenting to cardiologist 1 to 3 years after MI. In this retrospective post-hoc analysis, patients were categorized in 2 groups according to the achievement or not of the LDL-C goal of 70 mg/dL. Univariable and multivariable logistic regression analyses were performed to identify the baseline features associate with LDL-C≥70 mg/dL. RESULTS: The study population included 903 patients (mean age 65.5 ± 11.5 years). Among them, LDL-C was ≥70 mg/dL in 474 (52.5%). Male sex (p = 0.031), hypertension (p = 0.024), prior percutaneous coronary intervention (p = 0.016) and high education level (p = 0.008) were higher in the LDL-C < 70 group. At multivariable analysis, low education level was an independent predictor of LDL-C≥70 mg/dL (OR:1.582; 95%CI, 1.156-2.165; p = 0.004). Conversely, hypertension increased the probability to achieve the LDL-C goal (OR:0.650; 95%CI, 0.443-0.954; p = 0.028). Among off-target patients, LLT was not modified in the majority of cases (67.3%), intensified in 85 (18.6%), and actually reduced in 63 patients (13.8%). CONCLUSIONS: In patients presenting to cardiologists 1 to 3 years from the last MI event, LDL-C is not under control in a large proportion of patients, particularly in those with a low education level or without hypertension. LLT is underused in this very-high-risk setting.

[33] *Rikabi GE, Story LJ, Rikabi K*. **Patient-Centered Care: Lifestyle Modifications Among Adult Participants With Dyslipidemia**. J Dr Nurs Pract 2019; 12:31-40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32745053

ABSTRACT

BACKGROUND: Dyslipidemia, a risk factor for coronary heart disease (CHD), is a burden due to morbidity, mortality, and CHD-related costs. Patient-centered clinical interventions improve adherence to lifestyle modifications among adults with dyslipidemia. OBJECTIVE: The study's objectives were to (a) promote participants' safety through increased knowledge on the risks and prevention of CHD, (b) help participants identify their own barriers to lifestyle modifications, and (c) develop strategies with participants on individualized plans to adhere to healthy living. METHODS: Seventeen participants with dyslipidemia enrolled in a quality improvement over 6 weeks. Participants were from one employee health clinic in Mississippi. Measures are Heart Disease Fact Questionnaire (HDFQ), Framingham Tool, pre- and poststudy lipid panels, and physiologic measurements. Interventions include motivational technique-led interviews as a tool for behavioral change. RESULTS: Pre- and post-HDFQ responses indicated an 18% increase in knowledge attainment because of the patient-centered care interventions. Postinterventions, mean plasma lipid panels were 29% lower, weight loss ranged from 0 to 10.1 pounds, and body mass indexes were 0.4 to 1.2 less. Blood pressures (BPs) preintervention ranged from 120/70 to 159/89. Postinterventions BP ranged from 107/82 to 146/70. CONCLUSIONS: Patient-centered clinical interventions improve management of dyslipidemia through increased knowledge on risks and prevention of CHD and also through finding own barriers to healthy living. IMPLICATIONS: Healthcare providers can make a difference in people's lives through exploring the unhealthy behaviors and discovering ways for better health outcomes.

[34] *Rallidis LS, Iordanidis D, Iliodromitis E*. **The value of physical signs in identifying patients with familial hypercholesterolemia in the era of genetic testing**. J Cardiol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32741655
ABSTRACT
Familial hypercholesterolemia (FH) is a common, inherited disorder of cholesterol metabolism characterized by very high plasma concentrations of low-density lipoprotein cholesterol. It is crucial to diagnose and treat this disorder early since if left untreated it increases the risk for coronary artery disease (CAD) at least by 10-fold. Although genetic testing for FH, when available and affordable, should ideally be offered to most individuals with clinical phenotype suggestive of FH, it is underutilized in most countries. Therefore, FH diagnosis in the majority of cases is made by combining cholesterol levels and clinical characteristics of the patient leaving the need for genetic testing usually in equivocal cases. The presence of some cutaneous and ocular signs can raise the suspicion or even lead to the diagnosis of FH among usually "healthy" individuals. These physical signs comprise cutaneous lesions such as tendon xanthomas or the less specific xanthelasmata and ocular signs, such as corneal arcus in individuals under the age of 45 years. The presence of these signs should prompt the physician to request lipid tests and use clinical scores to diagnose FH. If the diagnosis of FH is likely, aggressive lipid-lowering therapy should be initiated to reduce the risk of CAD and a cascade screening of family members should also be requested.

[35] *McComb M, Krikheli M, Uher T et al.* **Neuroprotective associations of apolipoproteins A-I and A-II with neurofilament levels in early multiple sclerosis**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32758395
ABSTRACT
BACKGROUND: The role of cholesterol homeostasis in neuroaxonal injury in multiple sclerosis is not known. OBJECTIVE: The objective of the study is to investigate the associations of cerebrospinal fluid (CSF) and serum neurofilament light chain levels (CSF-NfL and sNfL, respectively), which are biomarkers of neuroaxonal injury, with cholesterol biomarkers at the clinical onset of multiple sclerosis. METHODS: sNfL, serum cholesterol profile (total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), serum apolipoprotein (Apo) levels (ApoA-I, ApoA-II, ApoB, and ApoE), and albumin quotient were obtained for 133 patients (63% female, age: 29.9 ± 8.0 years) during the first demyelinating event. CSF-NfL was available for 103 (77%) patients. RESULTS: CSF-NfL and sNfL were negatively associated with serum ApoA-II ($P = .005$, $P < .001$) and positively associated with albumin quotient ($P < .001$, $P < .0001$). In addition, higher CSF-NfL was associated with lower serum ApoA-I ($P = .009$) levels and higher sNfL was associated with lower high-density lipoprotein cholesterol ($P = .010$). In stepwise regression, age ($P = .045$), serum ApoA-II ($P = .022$), and albumin quotient ($P < .001$) were associated with CSF-NfL; albumin quotient ($P = .002$) and ApoA-II ($P = .001$) were associated with sNfL. Path analysis identified parallel pathways from ApoA-II ($P = .009$) and albumin quotient ($P < .001$) to the sNfL outcome that were mediated by CSF-NfL ($P < .001$). The associations of CSF-NfL with ApoA-I ($P = .014$) and ApoA-II ($P = .015$) and sNfL with ApoA-II ($P < .001$) remained significant after adjusting for number of contrast-enhancing lesions and T2 lesion volume. CONCLUSION: Lower serum

ApoA-II and ApoA-I levels are associated with greater neuroaxonal injury as measured by CSF-NfL.

[36] *Leopold JA*. **PCSK9 and Calcific Aortic Valve Stenosis: Moving Beyond Lipids**. JACC. Basic to translational science 2020; 5:662-664.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32760918
ABSTRACT
[Figure: see text]
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[37] *Gynnild MN, Aakerøy R, Spigset O et al.* **Vascular risk factor control and adherence to secondary preventive medication after ischaemic stroke**. Journal of internal medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32743852
ABSTRACT
BACKGROUND: Studies regarding adequacy of secondary stroke prevention are limited. We report medication adherence, risk factor control and factors influencing vascular risk profile following ischaemic stroke. METHODS: A total of 664 home-dwelling participants in the Norwegian Cognitive Impairment After Stroke study, a multicenter observational study, were evaluated 3 and 18 months poststroke. We assessed medication adherence by self-reporting (4-item Morisky Medication Adherence Scale) and medication persistence (defined as continuation of medication(s) prescribed at discharge), achievement of guideline-defined targets of blood pressure (BP) (<140/90 mmHg), low-density lipoprotein cholesterol (LDL-C) (<2.0 mmol L(-1)) and haemoglobin A1c (HbA1c) (≤53 mmol mol(-1)) and determinants of risk factor control. RESULTS: At discharge, 97% were prescribed antithrombotics, 88% lipid-lowering drugs, 68% antihypertensives and 12% antidiabetic drugs. Persistence of users declined to 99%, 88%, 93% and 95%, respectively, at 18 months. After 3 and 18 months, 80% and 73% reported high adherence. After 3 and 18 months, 40.7% and 47.0% gained BP control, 48.4% and 44.6% achieved LDL-C control, and 69.2% and 69.5% of diabetic patients achieved HbA1c control. Advanced age was associated with increased LDL-C control (OR 1.03, 95% CI 1.01 to 1.06) and reduced BP control (OR 0.98, 0.96 to 0.99). Women had poorer LDL-C control (OR 0.60, 0.37 to 0.98). Polypharmacy was associated with increased LDL-C control (OR 1.29, 1.18 to 1.41) and reduced HbA1c control (OR 0.76, 0.60 to 0.98). CONCLUSION: Risk factor control is suboptimal despite high medication persistence and adherence. Improved understanding of this complex clinical setting is needed for optimization of secondary preventive strategies.

[38] *Engel BJ, Preusch K, Brown C et al.* **Measurement of bempedoic acid and its keto metabolite in human plasma and urine using solid phase extraction and electrospray LC-MS/MS**. Journal of chromatography. B, Analytical technologies in the biomedical and life sciences 2020; 1154:122291.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32763847
ABSTRACT
Bempedoic acid, a new therapeutic for treatment of hypercholesterolemia, inhibits hepatic ATP-citrate lyase in the cholesterol synthesis pathway after its conjugation with coenzyme A. Sensitive and selective methods were required to study the pharmacokinetic behavior of

bempedoic acid and its active 8-keto metabolite in clinical studies. A mixed mode anion exchange extraction on 96-well plates was developed to favor high, selective recoveries of these dicarboxylic acids from urine or plasma. Adsorptive losses in urine led to inaccurate measurements unless samples were acidified and diluted with isopropanol prior to any specimen transfers. Tandem mass spectrometry with negative ion electrospray ionization permitted lower limits of measurement of 20 and 10 ng/mL for the drug and metabolite in either matrix. The methods were validated to current regulatory standards and have been the basis for pharmacokinetic measurements in 26 clinical studies involving over 15,000 samples.

[39] *Desikan SP, Sobash P, Fisher A, Desikan R*. **Statin-Induced Rhabdomyolysis Due to Pharmacokinetic Changes From Biliary Obstruction in a Patient With Metastatic Prostate Cancer**. Journal of investigative medicine high impact case reports 2020; 8:2324709620947275.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32755252
ABSTRACT
Statins work synergistically with androgen receptor blockers and androgen biosynthesis inhibitors, improving survival in patients with metastatic castration resistant prostate cancers (mCRPCs). Survival improvement is more pronounced for patients receiving androgen biosynthesis inhibitors compared with patients receiving androgen receptor blockers. A rare adverse interaction between simvastatin and abiraterone (Zytiga), an androgen biosynthesis inhibitor, was observed in a patient with mCRPC due to pharmacokinetic changes resulting from obstructive jaundice.

[40] *Crafa A, Condorelli RA, Mongioì LM et al.* **Mean Platelet Volume as a Marker of Vasculogenic Erectile Dysfunction and Future Cardiovascular Risk**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759752
ABSTRACT
Cardiovascular diseases are the main cause of mortality in the Western population, so the attempt to find a marker capable of predicting their early onset is not surprising. It is known that arteriogenic erectile dysfunction (ED) precedes the onset of a major coronary event by several years. However, a marker that is able to early identify those patients who should undergo further diagnostic investigations is, to date, missing. Recent research on this topic has focused on the role of the mean platelet volume (MPV), a marker of platelet activity that is high in most vascular diseases, such as coronary artery disease (CAD), stroke, peripheral artery disease (PAD), and ED. The basic pathophysiological mechanism of all these clinical conditions is atherosclerosis. Platelets play a central role in amplifying this process both indirectly by stimulating endothelial cells to produce inflammatory cytokines and chemokines, and directly through the expression of membrane receptors and the release of molecules that contribute to the formation of atherosclerotic plaque. The objective of this review is to critically analyze the evidence on the role of MPV in predicting the diagnosis and severity of vasculogenic ED and the possibility of using this simple marker as a first step to start a diagnostic process aimed at assessing the cardiovascular risk in these patients.

[41] *Chandra NC*. **Atherosclerosis and carcinoma: Two facets of dysfunctional cholesterol homeostasis**. Journal of biochemical and molecular toxicology 2020:e22595.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32761975

ABSTRACT

Although cholesterol is an essential and necessary component for biological systems; inappropriate accumulation of cholesterol in blood vessels and intracellular territory is also detrimental to living things. On one hand, cholesterol is the acting precursor of many metabolic regulators, a component of the structural veracity and scaffold fluidity of biomembranes, an insulator of electrical transmission in nerves and many more; on the other hand, its deposition in blood vessels induces atherosclerotic plaque and cardiovascular complications with the consequences of heart attack and stroke. It is also an emerging fact that cholesterol is a prelate in the cell nucleus for cell proliferation and any oddity in this venture may be the cause of tumorigenesis. Hence, cholesterol homeostasis is a very crucial element in issues of health management. Cholesterol is now a global target for maintaining quality health, particularly to control the two giants of the present world health tragedy: atherosclerosis and carcinoma, which appear to be the two facets of dysfunctional cholesterol homeostasis.

[42] *Zeitouni M, Nanna MG, Sun JL et al.* **Performance of Guideline Recommendations for Prevention of Myocardial Infarction in Young Adults**. Journal of the American College of Cardiology 2020; 76:653-664.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762899

ABSTRACT

BACKGROUND: The 2018 cholesterol guidelines of the American Heart Association and the American College of Cardiology (AHA/ACC) changed 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor (statin) eligibility criteria for primary prevention to include multiple risk enhancers and novel intensive lipid-lowering therapies for secondary prevention.
OBJECTIVES: This study sought to determine how guideline changes affected identification for preventive therapy in young adults with premature myocardial infarction (MI). METHODS: The study identified adults presenting with first MI at Duke University Medical Center in Durham, North Carolina. Statin therapy eligibility was determined using the 2013 ACC/AHA and 2018 AHA/ACC guidelines criteria. The study also determined potential eligibility for intensive lipid-lowering therapies (very high risk) under the 2018 AHA/ACC guidelines, by assessing the composite of all-cause death, recurrent MI, or stroke rates in adults considered "very high risk" versus not. RESULTS: Among 6,639 patients with MI, 41% were <55 years of age ("younger"), 35% were 55 to 65 years of age ("middle-aged"), and 24% were 66 to 75 years of age ("older"). Younger adults were more frequently smokers (52% vs. 38% vs. 22%, respectively) and obese (42% vs. 34% vs. 31%, respectively), with metabolic syndrome (21% vs. 19% vs. 17%, respectively) and higher low-density lipoprotein cholesterol (117 vs. 107 vs. 103 mg/dl, respectively) (p trend <0.01 for all). Pre-MI, fewer younger adults met guideline indications for 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor (statin) therapy than middle-aged and older adults. The 2018 guideline identified fewer younger adults eligible for statin therapy at the time of their MI than the 2013 guideline (46.4% vs. 56.7%; p < 0.01). Younger patients less frequently met very high-risk criteria for intensive secondary prevention lipid-lowering therapy (28.3% vs. 40.0% vs. 81.4%, respectively; p < 0.01). Over a median 8 years of follow-up, very high-risk criteria were associated with increased risk of major adverse cardiovascular events in individuals <55 years of age (hazard ratio: 2.09; 95% confidence interval: 1.82 to 2.41; p < 0.001), as was the case in older age groups (p interaction = 0.54).
CONCLUSIONS: Most younger patients with premature MI are not identified as statin

candidates before their event on the basis of the 2018 guidelines, and most patients with premature MI are not recommended for intensive post-MI lipid management.

[43] *Wang J, Qu HQ, Huang K et al.* **High prevalence of elevated serum liver enzymes in Chinese children suggests metabolic syndrome as a common risk factor**. J Paediatr Child Health 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32767607
ABSTRACT
AIM: This study investigated the pattern of liver enzymes in a large cohort of Chinese children and adolescents, including 16 383 individuals aged 4-18 years old recruited at six medical centres in China. METHODS: Clinical data were collected including weight, height, blood pressure, alanine aminotransferase, aspartate aminotransferase and fasting lipid panel. We used an unsupervised machine learning algorithm, the K-means clustering method, to identify different patterns of increased liver enzymes. RESULTS: Six clusters of elevated enzymes patterns were identified. The most common in 2.18% (325) of youth was elevated transaminases in the absence of features of metabolic syndrome(MetS), and they were thinner, and more likely to be from urban areas. The second cluster, with 1.47% (n = 220) youth had the most notable MetS features. They were older, obese and had central obesity, higher BP, triglycerides cholesterol and lower high-density lipoprotein cholesterol. Cluster 3 (0.6%, N = 90) had mild MetS, and cluster 4 (0.06%, N = 9), 5 (0.03%, N = 5) and 6 (0.007%, N = 1) were not related to MetS. CONCLUSIONS: We identified two distinct groups of children with both increased liver enzymes and MetS features in this population sample of Chinese children. One of the two groups had increased liver enzymes as the predominant clinical features at a younger age, suggesting genetic susceptibility to the condition. Further work to understand the increased MetS risk in cluster 2 is warranted.

[44] *Waldman HS, Smith JW, Lamberth J et al.* **A 28-Day Carbohydrate-Restricted Diet Improves Markers of Cardiovascular Disease in Professional Firefighters**. Journal of strength and conditioning research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32740289
ABSTRACT
Waldman, HS, Smith, JW, Lamberth, J, Fountain, BJ, Bloomer, RJ, Butawan, MB, and McAllister, MJ. A 28-day carbohydrate-restricted diet improves markers of cardiovascular disease in professional firefighters. J Strength Cond Res XX(X): 000-000, 2020-This study compared the effects of a 4-week, nonketogenic, carbohydrate-restricted (<25% of calories) diet (CRD) on markers of inflammation and oxidative stress in professional firefighters (FF). Subjects (n = 15) reported to the laboratory for 2 sessions (i.e., baseline and post-CRD) where blood was drawn from an antecubital vein after a 10-hour overnight fast. Dependent variables measured at baseline and post-CRD included adiponectin, insulin, human growth hormone, cortisol, C-reactive protein, albumin, lipids, glucose, amylase, creatine kinase, malondialdehyde (MDA), advance oxidation protein products (AOPP), total nitrate + nitrite, and soluble intracellular adhesion molecule-1. Compared with baseline, the CRD resulted in dramatic improvements to subjects' cardiometabolic profiles, including decreases in AOPP (51.3 ± 27.3 vs. 32.9 ± 7.9 ng·ml), MDA (1.6 ± 0.6 vs. 1.1 ± 0.5 μmol·L), and triglycerides (84.4 ± 34.4 vs. 64.2 ± 14.4 mg·dl), respectively. In addition, the CRD increased total cholesterol (151.5 ± 23.0 vs. 167.7 ± 38.2 mg·dl) and high-density lipoprotein cholesterol (46.3 ± 12.7 vs.

50.6 ± 15.5 mg·dl), but no differences were found with low-density lipoprotein cholesterol. Overall, our results show a 4-week CRD can favorably improve some markers of cardiovascular health in male FF.

[45] *Molina-Jijon E, Gambut S, Macé C et al.* **Secretion of the epithelial sodium channel chaperone PCSK9 from the cortical collecting duct links sodium retention with hypercholesterolemia in nephrotic syndrome**. Kidney international 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32750454
ABSTRACT
The proprotein PCSK9 functions as a chaperone for the epithelial sodium channel in the cortical collecting duct (CCD), is highly expressed in the liver, and plays a significant role in the pathogenesis of hypercholesterolemia. Lower levels of PCSK9 expression also occur in the normal kidney and intestine. Here, we found increased PCSK9 expression in the CCD of biopsies of patients with primary glomerular disease and explored a possible relationship with hypercholesterolemia of nephrotic syndrome. Significantly elevated serum PCSK9 and cholesterol levels were noted in two models of focal and segmental glomerulosclerosis, the Rrm2b-/- mouse and the Buffalo/Mna rat. Increased expression of PCSK9 in the kidney occurred when liver expression was reduced in both models. The impact of reduced or increased PCSK9 in the CCD on hypercholesterolemia in nephrotic syndrome was next studied. Mice with selective deficiency of PCSK9 expression in the collecting duct failed to develop hypercholesterolemia after injection of nephrotoxic serum. Blocking epithelial sodium channel activity with Amiloride in Rrm2b-/- mice resulted in increased expression of its chaperone PCSK9 in the CCD, followed by elevated plasma levels and worsening hypercholesterolemia. Thus, our data suggest that PCSK9 in the kidney plays a role in the initiation of hypercholesterolemia in nephrotic syndrome and make a case for depletion of PCSK9 early in patients with nephrotic syndrome to prevent the development of hypercholesterolemia.

[46] *Marchini JF, Manica A, Crestani P et al.* **Oxidized Low-Density Lipoprotein Induces Macrophage Production of Prothrombotic Microparticles**. Journal of the American Heart Association 2020; 9:e015878.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32750308
ABSTRACT
Background Activated vascular cells produce submicron prothrombotic and proinflammatory microparticle vesicles. Atherosclerotic plaques contain high levels of microparticles. Plasma microparticle levels increase during acute coronary syndromes and the thrombotic consequences of plaque rupture likely involve macrophage-derived microparticles (MΦMPs). The activation pathways that promote MΦMP production remain poorly defined. This study tested the hypothesis that signals implicated in atherogenesis also stimulate MΦMP production. Methods and Results We stimulated human primary MΦs with proinflammatory cytokines and atherogenic lipids, and measured MΦMP production by flow cytometry. Oxidized low-density lipoprotein (oxLDL; 25 μg/mL) induced MΦMP production in a concentration-dependent manner (293% increase; $P<0.001$), and these oxLDL MΦMP stimulatory effects were mediated by CD36. OxLDL stimulation increased MΦMP tissue factor content by 78% ($P<0.05$), and oxLDL-induced MΦMP production correlated with activation of caspase 3/7 signaling pathways. Salvionolic acid B, a CD36 inhibitor and a CD36 inhibitor antibody reduced

oxLDL-induced MΦMP by 67% and 60%, respectively. Caspase 3/7 inhibition reduced MΦMP release by 52% (P<0.01) and caspase 3/7 activation increased MΦMP production by 208% (P<0.01). Mevastatin pretreatment (10 μM) decreased oxLDL-induced caspase 3/7 activation and attenuated oxLDL-stimulated MΦMP production and tissue factor content by 60% (P<0.01) and 43% (P<0.05), respectively. Conclusions OxLDL induces the production of prothrombotic microparticles in macrophages. This process depends on caspases 3 and 7 and CD36 and is inhibited by mevastatin pretreatment. These findings link atherogenic signaling pathways, inflammation, and plaque thrombogenicity and identify a novel potential mechanism for antithrombotic effects of statins independent of LDL lowering.

[47] *Lin YC, Chen YC, Horng JT, Chen JM*. **Association of Fenofibrate and Diabetic Retinopathy in Type 2 Diabetic Patients: A Population-Based Retrospective Cohort Study in Taiwan**. Medicina (Kaunas, Lithuania) 2020; 56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32751875
ABSTRACT
Background and Objectives: Fenofibrate, a PPAR-α agonist, has been demonstrated to reduce the progression of diabetic retinopathy (DR) and the need for laser treatment in a FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) study. However, in the subgroup of patients without pre-existing DR, there was no significant difference in the progression of DR between the fenofibrate group and the placebo group. In this study, we aim to investigate whether fenofibrate can decrease the risk of incident DR in a population-based cohort study of type 2 diabetic patients in Taiwan. Materials and Methods: A total of 32,253 type 2 diabetic patients without previous retinopathy were retrieved from 892,419 patients in 2001-2002. They were then divided into two groups based on whether they were exposed to fenofibrate or not. The patients were followed until a diagnosis of diabetic retinopathy was made or until the year 2008. Results: With a follow-up period of 6.8 ± 1.5 years and 5.4 ± 2.6 years for 2500 fenofibrate users and 29,753 non-users, respectively, the Cox proportional hazard regression analysis revealed that the hazard ratio (HR) of new onset retinopathy was 0.57 (95% CI 0.57-0.62, p < 0.001). After adjusting for hypertension; the Charlson comorbidity index (CCI); and medications such as angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), anticoagulants, gemfibrozil, statins, and hypoglycemic agents, the adjusted HR was 0.75 (95% CI 0.68-0.82, p < 0.001). The need for laser treatment has an HR and adjusted HR of 0.59 (95% CI 0.49-0.71, p < 0.001) and 0.67 (95% CI 0.56-0.81, p < 0.001), respectively. Conclusion: Our study showed that the long-term and regular use of fenofibrate may decrease the risk of incident retinopathy and the need for laser treatment in type 2 diabetic patients. Since there are limitations associated with our study, further investigations are necessary to confirm such an association.

[48] *Janowski K, Obrycki Ł, Litwin M et al.* **Cardiovascular Risk Assessment in Children with Chronic Cholestatic Liver Diseases**. Journal of pediatric gastroenterology and nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32740536
ABSTRACT
OBJECTIVES: Chronic cholestatic liver diseases are often associated with disturbed lipid metabolism, which may potentially increase cardiovascular (CV) risk, but the evidence is scarce. The aim of the study was to assess factors associated with increased CV risk in

children with Alagille syndrome (AGS) and biliary atresia (BA). METHODS: We investigated 17 patients with AGS aged 11.0y (8.4-13.4) and 19 with BA aged 13.5y (10.4-15.1) in whom we performed thorough biochemical assessment including lipid profiles and oxidative stress biomarkers, blood pressure (BP)- systolic, diastolic and mean, carotid intima-media-thickness (cIMT) and pulse wave velocity (PWV). RESULTS: There were abnormal lipid profiles in 82% of children with AGS and 52.6% with BA. In AGS group we observed significantly higher levels of TC, LDL C, APO B, lower glutathione concentration and glutathione peroxidase activity and lower blood pressure, lower cIMT (p=0.02), cIMT-SDS (p=0.04) and PWV (p=0.04). However, we observed elevated blood pressure in 2/19 patients with BA and none-with AGS (BA vs AGS: p=0.12), while cIMT-SDS was increased only in 2/17 patients with AGS and in 6/19 with BA (p=0.24) and abnormal PWV-SDS values were detected in 3/17 of AGS and 8/19 of BA patients (p=0.15). Neither presence of dyslipidemia nor Lp-X correlated with vascular parameters. CONCLUSIONS: Children with BA and AGS may present with increased cardiovascular risk factors but vascular parameters are not directly related to lipid abnormalities. cIMT and BP should be considered for clinical practice in these cholestatic disorders so as to determine individuals with potential CV risk.

[49] *Hua S, Isasi CR, Kizer JR et al.* **Underuse of Cardiovascular Medications in Individuals With Known Lower Extremity Peripheral Artery Disease: HCHS/SOL**. Journal of the American Heart Association 2020; 9:e015451.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32752978
ABSTRACT
Background Underuse of cardiovascular medications for secondary prevention among individuals with peripheral artery disease (PAD) has been reported. Little is known about PAD treatment status in the Hispanic/Latino population in the United States, who may have limited access to health care and who have worse clinical outcomes than non-Hispanic individuals. Methods and Results We studied the use of cardiovascular therapies in 1244 Hispanic/Latino individuals recruited from 4 sites in the United States, including 826 individuals who reported diagnosis of PAD by physician and 418 individuals with coronary artery disease alone, in the Hispanic Community Health Study/Study of Latinos. We compared the prevalence of using antiplatelet therapy, lipid-lowering therapy and antihypertensive therapy by PAD and coronary artery disease status. Among those with PAD, we studied factors associated with taking cardiovascular medications, including demographic and socioeconomic factors, acculturation, access to health care and comorbidities, using multivariable regression models. The overall prevalence for individuals with PAD taking antiplatelet therapy, lipid-lowering therapy and, among hypertensive individuals, antihypertensive therapy was 31%, 26% and 57%, respectively. Individuals of Mexican background had the lowest use for all classes of cardiovascular medications. Older age, number of doctor visits and existing hypertension and diabetes mellitus were significantly associated with taking cardiovascular therapies in adjusted models. Compared with those with PAD alone, individuals with PAD and concurrent coronary artery disease were 1.52 (95% CI, 1.20-1.93) and 1.74 (1.30-2.32) times more likely to use antiplatelet agents and statins according to multivariable analysis. No significant difference of antihypertensive medication use was found among PAD patients with or without coronary artery disease. Conclusions Hispanic/Latino individuals with known PAD underuse cardiovascular medications recommended in clinical guidelines. More efforts should be directed to improve treatment in this important group.

[50] *Hong W, Wei Z, Qiu Z et al.* **Atorvastatin promotes bone formation in aged apoE(-/-) mice through the Sirt1-Runx2 axis**. Journal of orthopaedic surgery and research 2020; 15:303.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762716
ABSTRACT
BACKGROUND: Statins are the most widely used drugs in elderly patients; the most common clinical application of statins is in aged hyperlipemia patients. There are few studies on the effects and mechanisms of statins on bone in elderly mice with hyperlipemia. The study is to examine the effects of atorvastatin on bone phenotypes and metabolism in aged apolipoprotein E-deficient (apoE(-/-)) mice, and the possible mechanisms involved in these changes. METHODS: Twenty-four 60-week-old apoE(-/-) mice were randomly allocated to two groups. Twelve mice were orally gavaged with atorvastatin (10 mg/kg body weight/day) for 12 weeks; the others served as the control group. Bone mass and skeletal microarchitecture were determined using micro-CT. Bone metabolism was assessed by serum analyses, qRT-PCR, and Western blot. Bone marrow-derived mesenchymal stem cells (BMSCs) from apoE(-/-) mice were differentiated into osteoblasts and treated with atorvastatin and silent information regulator 1 (Sirt1) inhibitor EX-527. RESULTS: The results showed that long-term administration of atorvastatin increases bone mass and improves bone microarchitecture in trabecular bone but not in cortical bone. Furthermore, the serum bone formation marker osteocalcin (OCN) was ameliorated by atorvastatin, whereas the bone resorption marker tartrate-resistant acid phosphatase 5b (Trap5b) did not appear obviously changes after the treatment of atorvastatin. The mRNA expression of Sirt1, runt-related transcription factor 2 (Runx2), alkaline phosphatase (ALP), and OCN in bone tissue were increased after atorvastatin administration. Western blot showed same trend in Sirt1 and Runx2. The in vitro study showed that when BMSCs from apoE(-/-) mice were pretreated with EX527, the higher expression of Runx2, ALP, and OCN activated by atorvastatin decreased significantly or showed no difference compared with the control. The protein expression of Runx2 showed same trend. CONCLUSIONS: Accordingly, the current study validates the hypothesis that atorvastatin can increase bone mass and promote osteogenesis in aged apoE(-/-) mice by regulating the Sirt1-Runx2 axis.

[51] *Ding XY, Yang ZY, Zhao LY, Zhao WH*. **Are Lipid Profiles in Middle Age Associated with Famine Exposure during Prenatal and Early Postnatal Period?** Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32751112
ABSTRACT
BACKGROUND: Undernutrition during early life may increase the risk of chronic diseases in adulthood, including dyslipidemia. Few investigations have confirmed the relationship between early life undernutrition and dyslipidemia in adulthood in China. OBJECTIVES: To assess the relationship between the Great Chinese Famine exposure during prenatal period or early postnatal period and lipid profiles in adulthood. DESIGN: Data were extracted from the China Nutrition and Health Survey (CNHS) in 2010-2012, which included the participants who experienced the Great Chinese Famine during early life. RESULTS: Participants who experienced the Great Chinese Famine in early postnatal period had a significantly higher prevalence of elevated total cholesterol (TC) (odds ratio: 1.60; 95% CI: 1.27, 2.02) than unexposed participants. Female (odds ratio: 1.71; 95% CI: 1.27, 2.31) were high risk than male

(odds ratio: 1.46; 95% CI: 1.01, 2.11) and physical inactivity group (odds ratio: 1.65; 95% CI: 1.18, 2.29) were high risk than adequate physical activity group (odds ratio: 1.58; 95% CI: 1.21, 2.07). Similar effect of famine exposure on elevated low-density lipoprotein cholesterol (LDL-C) was observed, except that no significant difference was found between adequate physical activity group and physical inactivity group. Participants who experienced the Great Chinese Famine in prenatal period had a significantly higher prevalence of lowed high-density lipoprotein cholesterol (HDL-C) (odds ratio: 1.19; 95% CI: 1.03, 1.37) than unexposed. Female were more likely to have lower HDL-C (odds ratio: 1.44; 95% CI: 1.18, 1.74), but not found in male. Participants with physical inactivity were more likely to have lower HDL-C (odds ratio: 1.28; 95% CI: 1.02, 1.61), but not found in adequate physical activity group. CONCLUSIONS: People who experienced the Great Chinese Famine during early life, especially in females and people physical inactivity, would impair of lipid profiles in later life. Healthy lifestyle like adequate physical activity may partially alleviate the adverse effects.

[52] *Curtis D*. **Analysis of exome-sequenced UK Biobank subjects implicates genes affecting risk of hyperlipidaemia**. Molecular genetics and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32747172
ABSTRACT
Rare genetic variants in LDLR, APOB and PCSK9 are known causes of familial hypercholesterolaemia and it is expected that rare variants in other genes will also have effects on hyperlipidaemia risk although such genes remain to be identified. The UK Biobank consists of a sample of 500,000 volunteers and exome sequence data is available for 50,000 of them. 11,490 of these were classified as hyperlipidaemia cases on the basis of having a relevant diagnosis recorded and/or taking lipid-lowering medication while the remaining 38,463 were treated as controls. Variants in each gene were assigned weights according to rarity and predicted impact and overall weighted burden scores were compared between cases and controls, including population principal components as covariates. One biologically plausible gene, HUWE1, produced statistically significant evidence for association after correction for testing 22,028 genes with a signed log10 p value (SLP) of -6.15, suggesting a protective effect of variants in this gene. Other genes with uncorrected $p < .001$ are arguably also of interest, including LDLR (SLP = 3.67), RBP2 (SLP = 3.14), NPFFR1 (SLP = 3.02) and ACOT9 (SLP = -3.19). Gene set analysis indicated that rare variants in genes involved in metabolism and energy can influence hyperlipidaemia risk. Overall, the results provide some leads which might be followed up with functional studies and which could be tested in additional data sets as these become available. This research has been conducted using the UK Biobank Resource.

[53] *Yaman S, Ozdemir D, Akman BT et al.* **Awareness, treatment rates, and compliance to treatment in patients with serum LDL cholesterol higher than 250 mg/dl, and possible, probable or definite familial hypercholesterolemia**. Postgraduate medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32744105
ABSTRACT
PURPOSE: Familial hypercholesterolemia (FH) is a genetic disease characterized by increased levels of low density lipoprotein cholesterol (LDL-C). It is underdiagnosed and undertreated despite relatively high prevalance and significant association with increased mortality. We aimed to determine treatment status and compliance in patients with LDL-C≥250 mg/dL and FH. DESIGN: Patients older than 18 years old and have a serum LDL-C≥250

mg/dL between January 2010-December 2016 were identified from the hospital database. A phone survey was performed. Demographic features, smoking status, alcohol use, exercise, cardiovascular disease (CVD), use of medication for dyslipidemia, and CVD and high cholesterol levels in the family were questioned. Dutch Lipid Clinical Network Criteria was used to classify patients. The study was registered to Clinicaltrials.gov in July 2020 (NCT04494464). RESULTS: 1365 patients with a LDL-C≥250 mg/dL were identified. Patients that could not be reached and who refused to interview were excluded and the data of 367 patients were analyzed. There were 248 (67.6%) female and 119 (32.4%) male patients and mean age was 50.52±11.66. LDL-C was ≥330 mg/dL in 50 (13.6%) and 250-329 mg/dL in 317 (86.4%) patients. Forty (10.9%) patients were classified as definite, 181 (49.3%) as probable and 146 (39.8%) as possible FH. 213 (58.0%) patients were not receiving lipid-lowering treatment, and 162 (76.1%) stated that medication was never recommended previously, 30 (14.1%) had stopped medication him/herself and 21 (9.8%) had stopped medication with the advice of the physician. Among patients with definite/probable FH, 84 (38.0%) had CVD and the rate of lipid-lowering drug use in these patients was 58.3%. CONCLUSION: A significant proportion of patients with LDL-C≥250 mg/dL were not taking lipid-lowering drugs. Similar with many other studies, diagnosis and treatment rates of FH patients were very low in our study. Further national studies are required to increase awareness of the disease in both physicians and patients.

[54] *Volk C, Brandsch C, Schlegelmilch U et al.* **Postprandial Metabolic Response to Rapeseed Protein in Healthy Subjects**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32751170
ABSTRACT
Plant proteins have become increasingly important for ecological reasons. Rapeseed is a novel source of plant proteins with high biological value, but its metabolic impact in humans is largely unknown. A randomized, controlled intervention study including 20 healthy subjects was conducted in a crossover design. All participants received a test meal without additional protein or with 28 g of rapeseed protein isolate or soy protein isolate (control). Venous blood samples were collected over a 360-min period to analyze metabolites; satiety was assessed using a visual analog scale. Postprandial levels of lipids, urea, and amino acids increased following the intake of both protein isolates. The postprandial insulin response was lower after consumption of the rapeseed protein than after intake of the soy protein ($p < 0.05$), whereas the postmeal responses of glucose, lipids, interleukin-6, minerals, and urea were comparable between the two protein isolates. Interestingly, the rapeseed protein exerted stronger effects on postprandial satiety than the soy protein ($p < 0.05$). The postmeal metabolism following rapeseed protein intake is comparable with that of soy protein. The favorable effect of rapeseed protein on postprandial insulin and satiety makes it a valuable plant protein for human nutrition.

[55] *van Boheemen L, van Beers-Tas MH, Kroese JM et al.* **Cardiovascular risk in persons at risk of developing rheumatoid arthritis**. PloS one 2020; 15:e0237072.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32745151
ABSTRACT
BACKGROUND: Rheumatoid arthritis (RA) is associated with an increased cardiovascular disease (CVD) risk which may start even before diagnosis. To explore this CVD risk prior to

RA, we determined multiple risk factors and two 10-year clinical risk scores in a cohort of individuals at-risk of RA. We also analyzed associations with arthritis development and autoantibody status and compared a subset of at-risk individuals to an age and sex matched seronegative control group. METHODS: In a cohort of 555 consecutive arthralgia patients positive for rheumatoid factor (RF) and / or anti-citrullinated protein antibody (ACPA) we retrospectively identified patients with preclinical arthritis (i.e. those who developed arthritis), and non-arthritis patients (those without arthritis development during maximum 5 years follow up). Demographics, CVD risk factors and the 10-year cardiovascular risk according to the SCORE and QRISK3 system were determined at baseline. RESULTS: Preclinical arthritis patients (n = 188) had a higher heart rate (68 vs 63 bpm, p = 0.048) and lower cholesterol (5.2 mmol/l vs 5.5, p = 0.006), HDL (1.0 mmol/l vs 1.1, p0.003) and ApoB (0.85 g/l vs 0.91, p = 0.011) compared to non-arthritis patients (n = 367). Lipid levels were associated with ACPA status in both the preclinical arthritis and non-arthritis group. Ten-year CVD risk scores did not differ between preclinical arthritis and non-arthritis patients, in total, 7% (SCORE) and 8% (QRISK3) of seropositive arthralgia patients were classified as high risk. Seropositive at-risk patients (n = 71) had higher total cholesterol (5.4 vs 4.9, p<0.001), TC/HDL ratio (4.0 vs 3.0, p<0.001), triglycerides (1.4 vs 1.0, p = 0.001), ApoB (1.0 vs 0.9, p = 0.019) and 10-year risk scores (median SCORE 1.0 vs 0.0, p = 0.030 and median QRISK3 4.4 vs 3.1, p<0.001) compared to seronegative controls. CONCLUSION: Our results suggest that lipid changes commence prior to RA diagnosis and that ACPAs might play a role.

[56] *Valle M, St-Pierre P, Pilon G, Marette A*. **Differential Effects of Chronic Ingestion of Refined Sugars versus Natural Sweeteners on Insulin Resistance and Hepatic Steatosis in a Rat Model of Diet-Induced Obesity**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32751772

ABSTRACT

While the detrimental effect of refined sugars on health has been the subject of many investigations, little is known about the long-term impact of natural sweeteners on metabolic disorders. In this study we compared the metabolic responses to chronic ingestion of refined sugars compared to various natural sweeteners in diet-induced obese rats. Wistar rats were fed a high-fat high-sucrose diet (HFHS) for 8 weeks and daily gavaged with a solution containing 1 g of total carbohydrates from refined sugar (sucrose or fructose) or six different natural sugar sources, followed by assessment of glucose homeostasis, hepatic lipid accumulation, and inflammation. While glucose tolerance was similar following treatments with refined and natural sugars, lowered glucose-induced hyperinsulinemia was observed with fructose. Consumption of fructose and all-natural sweeteners but not corn syrup were associated with lower insulin resistance as revealed by reduced fasting insulin and homeostatic model assessment of insulin resistance (HOMA-IR) compared to sucrose treatment of HFHS-fed rats. All-natural sweeteners and fructose induced similar liver lipid accumulation as sucrose. Nevertheless, maple syrup, molasses, agave syrup, and corn syrup as well as fructose further reduced hepatic IL-1β levels compared to sucrose treatment. We conclude that natural sweeteners and especially maple syrup, molasses, and agave syrup attenuate the development of insulin resistance and hepatic inflammation compared to sucrose in diet-induced obese rats, suggesting that consumption of those natural sweeteners is a less harmful alternative to sucrose in the context of obesity.

[57] *Trivedi K, Le V, Nelson JR*. **The case for adding eicosapentaenoic acid (icosapent ethyl) to the ABCs of cardiovascular disease prevention**. Postgraduate medicine 2020:1-14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762268
ABSTRACT
The high-purity eicosapentaenoic acid (EPA) prescription fish oil-derived omega-3 fatty acid (omega-3), icosapent ethyl (IPE), was recently approved by the United States Food and Drug Administration (FDA) for cardiovascular disease (CVD) prevention in high-risk patients. This approval is based on the 25% CVD event risk reduction observed with IPE in the pre-specified primary composite endpoint (cardiovascular [CV] death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or hospitalization for unstable angina) in the landmark Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT). Notably, this reduction in CVD event risk with IPE was an incremental benefit to well-controlled low-density lipoprotein cholesterol; patients in REDUCE-IT had elevated triglyceride (TG) levels (135-499 mg/dL) and either had a history of atherosclerotic CVD or diabetes with additional CV risk factors. Given the CVD event risk reduction in REDUCE-IT, within a year following trial results, several global medical societies added IPE to their clinical guidelines. IPE is a stable, highly purified, FDA-approved prescription EPA ethyl ester. In contrast, mixed omega-3 products (docosahexaenoic acid + EPA combinations) have limited or no evidence for CVD event risk reduction, and nonprescription fish oil dietary supplements are not regulated as medicine by the FDA. We offer our perspective and rationale for why this evidence-based EPA-only formulation, IPE, should be added to the 'E' in the ABCDEF methodology for CV prevention. We provide multiple lines of evidence regarding an unmet need for CVD prevention beyond statin therapy, IPE clinical trials, IPE cost-effectiveness analyses, and proposed pleiotropic (non-lipid) mechanisms of action of EPA, as well as other relevant clinical considerations. See Figure 1 for the graphical abstract.[Figure: see text].

[58] *Landers-Ramos RQ, Addison OA, Beamer B et al.* **Circulating microparticle concentrations across acute and chronic cardiovascular disease conditions**. Physiological reports 2020; 8:e14534.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32748505
ABSTRACT
Concentrations of different circulating microparticles (MPs) may have clinical and physiological relevance to cardiovascular disease pathologies. PURPOSE: To quantify plasma concentrations of CD31+/CD42b-, CD62E+, and CD34+ MPs across healthy individuals and those with coronary artery disease (CAD) or acute cardiovascular events (non-ST elevation myocardial infarction (NSTEMI)). Fasted blood was obtained from CAD patients (n = 10), NSTEMI patients (n = 13), and healthy older men (n = 15) 60-75 years old. METHODS: CD31+/CD42b-, CD62E+, and CD34+ MPs were isolated from plasma and quantified using flow cytometry. Relationships between MP subtypes, fasting blood lipids, blood glucose, blood pressure, body mass index, and total number of medications were assessed. RESULTS: Concentrations of CD31+/CD42b- MPs were significantly lower in CAD and NSTEMI subjects compared with healthy individuals ($p = .02$ and $.003$, respectively). No differences between groups were found for CD62E+ or CD34+ MPs ($p > .05$ for both). Surprisingly, among all variables assessed, only CD62E+ MP concentrations were positively correlated with triglyceride levels ($p = .012$) and inversely correlated with SBP ($p = .03$). CONCLUSIONS: Our

findings provide support for the use of different MP subtypes, specifically CD31+/CD42b- MPs, as a potential biomarker of cardiovascular disease. Importantly, results from this study should be looked at in adjunct to previous MP work in CVD conditions as a way of highlighting the complex interactions of variables such as comorbid conditions and medications on MP concentrations.

[59] *Hofbauer S, Wiesli P*. **[CME: Primary and Secondary Hypercholesterolemia]**. Praxis 2020; 109:755-762.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32752965
ABSTRACT
CME: Primary and Secondary Hypercholesterolemia Abstract. In patients with hypercholesterolemia and an LDL-cholesterol level >5 mmol/l, familial hypercholesterolemia (primary hypercholesterolemia) should be considered. This genetically determined illness should lead to medical therapy and screening for hypercholesterinemia in close relatives. Beside the superelevated LDL-cholesterol levels, additional clinically diagnostic findings and family anamnesis can support the diagnosis of familial hypercholesterolemia. The likelihood of familial hypercholesterolemia can be estimated using the Lipid Clinic Network Score. Additionally, a variety of exogenous factors may have an impact on lipoprotein metabolism and may lead to secondary hypercholesterolemia. Hypothyroidism, cholestasis, nephrotic syndrome or specific medications, among others, should be considered as potential factors leading to high cholesterol levels before familial hypercholesterolemia is suspected or lipid-lowering treatment is started.

[60] *El-Khatib LA, De Feijter-Rupp H, Janoudi A et al.* **Cholesterol induced heart valve inflammation and injury: efficacy of cholesterol lowering treatment**. Open heart 2020; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32747455
ABSTRACT
BACKGROUND: Heart valves often undergo a degenerative process leading to mechanical dysfunction that requires valve replacement. This process has been compared with atherosclerosis because of shared pathology and risk factors. In this study, we aimed to elucidate the role of inflammation triggered by cholesterol infiltration and cholesterol crystals formation causing mechanical and biochemical injury in heart valves. METHODS: Human and atherosclerotic rabbit heart valves were evaluated. New Zealand White male rabbits were fed an enriched cholesterol diet alone or with simvastatin and ezetimibe simultaneous or after 6 months of initiating cholesterol diet. Inflammation was measured using C-reactive protein (CRP) and RAM 11 of tissue macrophage content. Cholesterol crystal presence and content in valves was evaluated using scanning electron microscopy. RESULTS: Cholesterol diet alone induced cholesterol infiltration of valves with associated increased inflammation. Tissue cholesterol, CRP levels and RAM 11 were significantly lower in simvastatin and ezetimibe rabbit groups compared with cholesterol diet alone. However, the treatment was effective only when initiated with a cholesterol diet but not after lipid infiltration in valves. Aortic valve cholesterol content was significantly greater than all other cardiac valves. Extensive amounts of cholesterol crystals were noted in rabbit valves on cholesterol diet and in diseased human valves. CONCLUSIONS: Prevention of valve infiltration with cholesterol and reduced inflammation by simvastatin and ezetimibe was effective only when given during the initiation

of high cholesterol diet but was not effective when given following infiltration of cholesterol into the valve matrix.

[61] *DiNicolantonio JJ, O'Keefe JH*. **The Importance of Marine Omega-3s for Brain Development and the Prevention and Treatment of Behavior, Mood, and Other Brain Disorders**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759851
ABSTRACT
Most of the global population is deficient in long-chain marine omega-3s. In particular, docosahexaenoic acid (DHA), a long-chain omega-3 fatty acid, is important for brain and eye development. Additionally, DHA plays a significant role in mental health throughout early childhood and even into adulthood. In the brain, DHA is important for cellular membrane fluidity, function and neurotransmitter release. Evidence indicates that a low intake of marine omega-3s increases the risk for numerous mental health issues, including Attention Deficit Hyperactivity Disorder (ADHD), autism, bipolar disorder, depression and suicidal ideation. Studies giving supplemental marine omega-3s have shown promise for improving numerous mental health conditions. This paper will review the evidence surrounding marine omega-3s and mental health conditions.

[62] *Bahia W, Soltani I, Haddad A et al.* **Contribution of ADIPOQ Variants to the Genetic Susceptibility of Recurrent Pregnancy Loss**. Reproductive sciences (Thousand Oaks, Calif.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32748222
ABSTRACT
Adiponectin is a hormone implicated in regulating energy, lipid, and glucose metabolism and is encoded by the ADIPOQ gene. ADIPOQ variants can regulate the circulating levels of adiponectin. Irregular adiponectin concentrations have been associated with numerous reproductive diseases including recurrent pregnancy loss (RPL). The main objective of this study was to determine whether the 14 selected polymorphisms of the ADIPOQ gene are linked with RPL. The retrospective case-control study comprised a total of 332 women with RPL, adjusted as more than three consecutive abortions of unknown etiology, and 286 healthy controls. They were genotyped for the ADIPOQ variants using allele exclusion method on real-time PCR. Significantly higher rs1501299 minor allele frequencies (MAF) and lower rs2241767 and rs2241766 MAF were seen among RPL women, thereby assigning disease susceptibility and protective aspect to the mentioned variants, respectively. Different associations of ADIPOQ genotypes with RPL were noticed according to the genetic model exploited: rs1501299 and rs2241767 were significantly linked with RPL under the three models, while rs17366568 and rs2241766 were associated with RPL under codominant and dominant models, and rs7649121 was related to RPL under the dominant and recessive models. rs4632532 was linked according to the recessive model only. Based on LD pattern, 2-haplotype blocks were specified. Reduced frequency of AGG and GAGG and increased frequency of TAAG were noted in cases, compared with controls, hence indicating these haplotypes as RPL-protective and RPL-susceptible, respectively. These results support a significant role of ADIPOQ as an RPL candidate locus.

[63] *Suzuki E, Oshima M, Sonotsuka M et al.* **[Effects of Medium Chain Triglycerides Intake on Lipid Metabolism and Intestinal Disaccharidase Activities in Rats]**. Yakugaku Zasshi 2020; 140:1051-1061.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32741863
ABSTRACT
It has been reported that medium-chain triglyceride (MCT) have various physiological functions, such as anti-obesity and hypolipidemic effects. They can also elicit increased disaccharidase activity and intestinal cell proliferation. However, a meta-analysis of randomized controlled trials, comparing the effects of MCT on weight loss and body composition, detected commercial bias. Additional research on the physiological functions is needed in order to have conclusive evidence. Thus, we sought to evaluate the various functions of MCT by conducting a feeding study in rats. Rats fed a diet containing 15% (w/w) MCT, had significantly lower visceral fat weight, plasma and liver lipid concentrations; they had significantly higher intestinal maltase and glucoamylase activities; and they had a greater number of Ki-67 positive cells/crypt, compared to the rats fed a diet containing 15% (w/w) lard. The effects of a diet containing 5% (w/w) MCT was observed only for plasma cholesterol levels and the number of Ki-67 positive cells/crypt; in which some results were found to be inconsistent with previous reports. These results indicate that physiological functions of MCT are numerous and need to be confirmed by additional research.

[64] *Możeńska O, Wojewódzki M, Wiligórska D et al.* **Conservative treatment as a therapeutic option for penetrating aortic ulcer of the aortic arch in a patient with bicuspid aortic valve**. Wiadomosci lekarskie (Warsaw, Poland : 1960) 2020; 73:1580-1582.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759458
ABSTRACT
Penetrating aortic ulcer (PAU) is ulceration of an aortic atherosclerotic plaque penetrating through the internal lamina into the media. PAU is a rare condition and occurs in 2% - 7% of acute aortic syndromes (AAS); however, the actual incidence is unknown because of asymptomatic patients. One may treat it conservatively as well as surgically. We present a case of a 54-year-old man, who was admitted to hospital due to the exaggeration of exertional chest pain and persistent headaches. During coronary angiography, the suspicion of PAU was raised. Contrast-enhanced computed tomography confirmed the diagnosis. Transesophageal echocardiography showed bicuspid aortic valve with minimal calcification, the dilated ascending aorta, large atherosclerotic plaques in the aortic arch with ulceration (thickness: 5.0 - 5.5mm, diameter: 5 - 6 mm, depth: 3 - 4 mm), without intramural hematoma. Conservative treatment was chosen with uneventful 2-year follow-up. Although surgical management is advocated for patients with PAU type A, we demonstrated that type A PAU can be successfully treated conservatively as well.

[65] *Dou K, Ye J, Zhang X, Luo J*. **[Development of a New Type of Atherosclerosis Detection Device]**. Zhongguo Yi Liao Qi Xie Za Zhi 2020; 44:311-314.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762203
ABSTRACT
This paper describes how to develop a practical new type of atherosclerosis detection device, which can realize real-time measurement and analysis of human atherosclerosis. According to the mechanism of human atherosclerosis, the design objectives of the system are formulated

to determine the construction of the platform. The system calculates the pulse wave velocity by measuring the pulse wave of human fingers and toes, adds four blood pressure measurements to the system design, calculates the ankle-brachial index, and comprehensively measures and analyses the degree of human arteriosclerosis.

[66] *Cowley E, Omar MA*. **Suspected Drug-Induced Rhabdomyolysis From the Combination of Atorvastatin, Amiodarone, and Ciprofloxacin**. The Annals of pharmacotherapy 2020:1060028020946299.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32762337
ABSTRACT

[67] *Ahmad MN, Farh AI, Al-Qirim TM*. **The Cardiovascular Complications of Diabetes: A Striking Link through Protein Glycation**. Romanian journal of internal medicine = Revue roumaine de medecine interne 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32759408
ABSTRACT
Diabetes mellitus is a predominant cause of mortality and morbidity worldwide. One of its serious health problems is cardiovascular complications. Advanced glycation end products (AGEs) are a group of heterogeneous toxic oxidant compounds that are formed after a nonenzymatic reaction between monosaccharides and free amino groups of proteins, compound lipids, and nucleic acids. AGE interacts with various types of cells through a receptor for AGE (RAGE). The interaction between AGE and RAGE is responsible for a cascade of inflammation, oxidative stress, and disruption of calcium homeostasis in cardiac cells of diabetic patients. There is striking evidence that the AGE/RAGE axis with its consequences on inflammation and oxidative stress plays a major role in the development of cardiovascular complications. Therefore, considering AGE as a therapeutic target with foreseeable results would be a wise direction for future research. Interestingly, several studies on nutraceutical, pharmaceutical, and natural products have begun to reveal promising therapeutic results, and this could lead to better health outcomes for many diabetic patients worldwide. This article discusses the current literature addressing the connection between protein glycation and diabetes cardiovascular complications and suggests future avenues of research.