Literature update week 36 (2018)

[1] *Li XX, Zhao L, Chang Y et al.* **Ezetimibe prevents myocardial remodeling in an obese rat model by inhibiting inflammation**. Acta biochimica Polonica 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30188965
ABSTRACT
Inflammation plays an important role in the development of many obesity-related diseases. This study aimed to investigate the effect of ezetimibe on inflammation and myocardial remodeling in obese rats. A rat model of obesity was established, and myocardial damage was examined by transmission electron microscopy and Masson staining. Twenty obese rats were divided into two groups (n=10): obese group and ezetimibe group. Ten SD rats were used as controls. Western blot was performed to monitor the expression of P-p38MAPK and interleukin (IL)-6. Immunohistochemical staining was used to monitor the expression of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1. In the obese rats group, we observed increased inflammatory factors and myocardial hypertrophy. In contrast, the ezetimibe group exhibited decreased expression of inflammatory factors and an improvement in myocardial remodeling compared to the obese group. Mechanistically, we found that ezetimibe decreased P-p38MAPK, IL-6, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1 levels in the hearts of the obese rats. Taken together, these results indicate that ezetimibe may improve myocardial remodeling in obese rats by inhibiting inflammation.

[2] *Ambrosy AP, Cerbin LP, Fudim M et al.* **Natural History of Patients Postacute Coronary Syndrome Based on Heart Failure Status**. The American journal of cardiology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30180960
ABSTRACT
The natural history of patients hospitalized for acute coronary syndrome (ACS) with pre-existing versus (vs) de novo heart failure (HF) has not been previously reported over an extended duration of follow-up. The IMPROVE-IT trial enrolled 18,144 patients hospitalized for ACS and randomized them to combination simvastatin (40 mg)/ezetimibe (10 mg) vs simvastatin (40 mg). Subjects were divided into 3 groups: pre-existing HF (i.e., defined by past medical history), de novo HF (i.e., defined by Killip class II or greater during index admission), and no HF. The final analytical cohort included 14,792 patients (82%) with HF status recorded at baseline. In total, 790 patients (5.3%) reported a pre-existing diagnosis of HF and 1374 patients (9.3%) experienced de novo HF. Patients with pre-existing or de novo HF were older, more likely to be woman, and had a greater prevalence of atrial fibrillation and diabetes mellitus. The incidences of death/HF-hospitalizations at 5 years were 32%/20% for pre-existing HF, 18%/7% for de novo HF, and 8%/3% for no HF. After adjusting for potential confounders, a history of pre-existing or de novo HF was independently associated with increased risk of death (pre-existing HF: hazard ratio [HR] 1.93, 95% confidence interval [CI] 1.68 to 2.22, $p < 0.001$; de novo HF: HR 1.51, 95% CI 1.33 to 1.72, $p < 0.001$) and hospitalizations for HF (pre-existing HF: HR 2.96, 95% CI 2.36 to 3.71, $p < 0.001$; de novo HF: HR 1.88, 95% CI 1.49 to 2.38, $p < 0.001$). There was no interaction among baseline HF status (i.e., pre-existing or de novo), lipid lowering therapy (i.e., simvastatin/ezetimibe vs simvastatin alone), and clinical outcomes. In conclusion, patients hospitalized for ACS with pre-existing or de novo HF were older and had a greater burden of medical co-morbidities. In conclusion, HF was independently associated with increased risk of

long-term morbidity and mortality with the pre-existing HF cohort demonstrating the highest overall risk.

[3] *Shomali T, Taherianfard M, Dalvand M, Namazi F*. **Effect of pharmacological doses of niacin on testicular structure and function in normal and diabetic rats**. Andrologia 2018:e13142.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30191583
ABSTRACT
Male diabetic patients may experience adverse changes in testicular functions or structure. Niacin has antidyslipidemic properties in diabetic patients. We aimed to clarify the effect of pharmacological doses of niacin on testicular structure and function of normal and diabetic rats. Sixty adult male rats were treated as follows. Healthy control (HC); diabetic control (DC); NL and NH groups: normal rats that received niacin at 800 and 4,000 mg/kg of diet; DL and DH groups: diabetic rats that received niacin at 800 and 4,000 mg/kg diet for 50 days. In normal rats, obvious increase in serum testosterone especially in NL group associated with improved antioxidant status of testicular tissue was observed. In diabetic rats, niacin resulted in higher testicular weight/body weight and improved some histological parameters without affecting blood glucose, testosterone and sperm count. Testicular MDA content decreased. In conclusion, niacin especially at 800 mg/kg diet improves serum testosterone levels and antioxidant status of testes in normal rats. In diabetic rats, despite positive changes in histological features and antioxidant status of testes reproductive outcome including sperm count or testosterone levels were not improved. This study set the scene for further investigations on the effect of niacin on male reproductive system.

[4] *Chen W, Yu F, Di M et al.* **MicroRNA-124-3p inhibits collagen synthesis in atherosclerotic plaques by targeting prolyl 4-hydroxylase subunit alpha-1 (P4HA1) in vascular smooth muscle cells**. Atherosclerosis 2018; 277:98-107.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30193190
ABSTRACT
BACKGROUND AND AIMS: Collagen synthesis in vascular smooth muscle cells (VSMCs) is very important in atherosclerosis, as it affects plaque stability. In this study, we aim to assess whether miR-124-3p is involved in the collagen synthesis process in VSMCs and the role it might play in atherosclerotic development. METHODS: We modulated the miR-124-3p expression in the aortic root plaques of high-fat-diet fed ApoE(-/-) mice by lentivirus injection. To determine plaque size and the content of plaque-stability-related cells or molecules, stainings, including hematoxylin and eosin, Oil red O, Sirius Red and immunohistochemical staining, were performed. Fluorescence in situ hybridization (FISH) was used to locate miR-124-3p in atherosclerotic plaques. Western blotting and RT-qPCR were carried out to determine the level of P4HA1 as well as type I and type III collagen protein and mRNA expression. RESULTS: Results showed that collagen and VSMC content of plaques was inversely correlated with miR-124-3p levels. By FISH, we identified that miR-124-3p was primarily expressed by VSMCs. We also found that protein levels of type I and type III collagen in aortas and atherosclerotic plaques were decreased by miR-124-3p. We modulated miR-124-3p level in vitro and found it could inhibit collagen expression in HASMCs. This might be caused by the downregulation of P4HA1. P4HA1 was predicted as miR-124-3p's direct target, which was verified with a dual luciferase

reporter assay and RIP test. CONCLUSIONS: The results presented here provide evidence that miR-124-3p inhibits VSMC collagen synthesis by directly targeting P4HA1, which might decrease atherosclerotic plaque stability.

[5] *Cho KI, Sakuma I, Sohn IS et al.* **Inflammatory and metabolic mechanisms underlying the calcific aortic valve disease**. Atherosclerosis 2018; 277:60-65.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30173080
ABSTRACT
Although calcific aortic stenosis is a very common disease with major adverse cardiovascular events and healthcare costs, there are no effective medical interventions to delay or halt its progression. Cardiometabolic risk factors, including smoking and male sex, are linked to aortic stenosis. Emerging studies have identified important regulatory roles for immunological and inflammatory responses, including oxidized lipids, various cytokines, and biomineralization. Recent clinical and experimental studies in atherosclerosis and osteoporosis have demonstrated that oxidative stress and oxidized lipids decrease bone formation in the skeletal system while they increase bone formation in the cardiovascular system. Multidisciplinary factors contribute to vascular calcification, including inflammation and metabolic regulation of osteogenesis in the cardiovascular system via similar signaling pathways as bone formation. Calcific aortic valve disease (CAVD) is no longer considered a simple passive process of calcium deposition that occurs with advanced age. Biomineralization in CAVD is a complex, regulated process that involves valvular, circulating, bone marrow-derived cells, macrophage heterogeneity and genetic factors along with biochemical and mechanical factors. The current review will discuss the recently discovered important role of inflammation, metabolic risk factors, and molecular and cellular mechanisms that promote CAVD, as well as the link between osteogenic signals in the skeletal and cardiovascular systems. This may inform future therapeutic strategies for CAVD progression.

[6] *Lutjohann D, Laufs U, Schulze CP, Weingartner O*. **Call for an ezetimibe effectiveness test**. Atherosclerosis 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30193821
ABSTRACT

[7] *Munoz-Hernandez L, Ortiz-Bautista RJ, Brito-Cordova G et al.* **Cholesterol efflux capacity of large, small and total HDL particles is unaltered by atorvastatin in patients with type 2 diabetes**. Atherosclerosis 2018; 277:72-79.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30176567
ABSTRACT
BACKGROUND AND AIMS: Research on the biologic activities of HDL, such as cholesterol efflux capacity and HDL composition, has allowed the understanding of the effect of interventions directed to improve cardiovascular risk. Previously, statin therapy has shown conflicting results about its effects on cholesterol efflux capacity of HDL; the underlying mechanisms are unclear but studies with positive effects are associated with an increase of HDL-cholesterol levels. We investigated if 10 weeks of atorvastatin therapy changes HDL efflux capacity and the chemical composition of its subpopulations. METHODS: In a before-after design basis, HDL-cholesterol

levels, chemical composition and cholesterol efflux capacity from HDL subpopulations isolated by isophynic ultracentrifugation were assessed in plasma samples from 60 patients with type 2 diabetes mellito (T2DM) at baseline and after 10 weeks of treatment with 20mg atorvastatin. Cholesterol efflux was measured from human THP-1cells using large, light HDL2b and small, dense 3c subpopulations as well as total HDL as acceptors. Changes of cholesterol efflux and chemical composition of HDL after treatment were analyzed. Correlations among variables potentially involved in cholesterol efflux were evaluated. RESULTS: A significant decrease of 4% in HDL-cholesterol levels was observed from 47 (42-54) to 45 (39-56) mg/dL, p=0.02. Cholesterol efflux from total-HDL and HDL2b and 3c subfractions was maintained unchanged after treatment. The total mass of HDL remained unaffected, except for the HDL3a subpopulation accounted for by a significant increase in total protein content. No significant correlations for variables previously known to be associated with cholesterol efflux were found in our study. CONCLUSIONS: Short therapy of 10 weeks with 20mg of atorvastatin does not modify the cholesterol efflux capacity neither the total mass of HDL2b, HDL3c and total HDL. The discrepancy with previous reports may be due to the selective effects among different classes of statins or differences in the approaches to measure cellular cholesterol efflux.

[8] *Oberoi R, Vlacil AK, Schuett J et al.* **Anti-tumor necrosis factor-alpha therapy increases plaque burden in a mouse model of experimental atherosclerosis**. Atherosclerosis 2018; 277:80-89.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30176568
ABSTRACT
BACKGROUND AND AIMS: Atherosclerosis is critically fueled by vascular inflammation through oxidized lipids and inflammatory cytokines such as tumor necrosis factor (TNF)-alpha. Genetic disruption of Tnf-alpha reduces atherosclerosis in experimental mouse models. However, less is known about the therapeutic potential of Tnf-alpha blockage by pharmacological inhibitors such as monoclonal antibodies, which are already approved for several inflammatory disorders in patients. Therefore, we investigated the effect of pharmacological TNF-alpha inhibition on plaque development in experimental atherosclerosis. RESULTS: 10 week old male Ldlr(-/-) mice were divided into 4 groups (n=7-10) and fed a high fat, high cholesterol diet for 6 and 12 weeks. Simultaneously, the mouse-specific anti-Tnf-alpha monoclonal antibody CNTO5048 (CNT) or a control IgG was administered. RESULTS: CNT reduced circulating inflammatory markers without affecting body weight and glucose metabolism. Unexpectedly, CNT treatment increased plasma triglyceride levels and pro-atherogenic very-low-density lipoprotein (VLDL) cholesterol as well as plaque burden in the thoracoabdominal aorta and in the aortic root. In addition, we observed decreased smooth muscle cell content in the lesions and a trend towards reduced collagen deposition upon Tnf-alpha inhibition. Furthermore, inflammatory gene expression in the aortic arch was increased following Tnf-alpha inhibitor treatment. CONCLUSIONS: Although up to 12-week pharmacological inhibition of TNF-alpha in Ldlr(-/-) mice diminishes systemic inflammation, experimental plaque burden and vascular inflammatory gene expression are increased, while markers of plaque stability decrease. These observations may be explained by the development of a pro-atherogenic plasma lipid profile.

[9] *Vinding RK, Stokholm J, Sevelsted A et al.* **Effect of fish oil supplementation in pregnancy on bone, lean, and fat mass at six years: randomised clinical trial**. Bmj 2018; 362:k3312.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30181143

ABSTRACT

OBJECTIVE: To examine the effect of supplementation with n-3 long chain polyunsaturated fatty acids (n-3 LCPUFA) in pregnancy on anthropometry and body composition in offspring. DESIGN: Double blinded, randomised controlled trial. SETTING: Copenhagen Prospective Studies on Asthma in Childhood2010 cohort. PARTICIPANTS: 736 pregnant women and their offspring. INTERVENTION: n-3 LCPUFA (fish oil) or control (olive oil) daily from pregnancy week 24 until one week after birth. MAIN OUTCOME MEASURES: Height/length, weight, head, and waist measurements and body composition from dual energy x ray absorptiometry (all pre-specified secondary endpoints of the n-3 LCPUFA trial; the primary outcome for the trial was persistent wheeze/asthma). RESULTS: The mean body mass index (BMI) z score was increased between age 0 and 6 years in the fish oil supplementation group compared with the control group (0.14 (95% confidence interval 0.04 to 0.23); P=0.006). At 6 years, supplementation was associated with a higher BMI z score (0.19 (0.06 to 0.32); P=0.004), a higher weight/height (3.48 (0.38 to 6.57) g/cm; P=0.03), and a larger waist circumference (0.6 (0.0 to 1.2) cm; P=0.04) but not a higher proportion of obese children, using International Obesity Task Force grades. The dual energy x ray absorptiometry scan at age 6 years showed a higher total mass (395.4 (86.6 to 704.3) g; P=0.01) in the supplementation versus the control group, explained by a higher lean mass (280.7 (98.9 to 462.4) g; P=0.002), a higher bone mineral content (10.3 (2.3 to 18.1) g; P=0.01), and a non-significantly higher fat mass (116.3 (-92.9 to 325.5) g; P=0.28), but no differences were seen in total body fat or lean mass percentage. CONCLUSION: Fish oil supplementation from the 24th week of pregnancy led to a higher BMI in the offspring from 0 to 6 years of age but not an increased risk of obesity at age 6. The body composition at age 6 years in children given fish oil supplementation was characterised by a proportional increase in lean, bone, and fat mass suggesting a general growth stimulating effect of n-3 LCPUFA. TRIAL REGISTRATION: Clinicaltrials.gov NCT00798226.

[10] *Zhang J, Shao Y, Liu Y, Tao J*. **A Multi-Center, Open-Label, Two-Arm Parallel Group Non-inferiority Randomized Controlled Trial Evaluating the Effect of Pitavastatin, Compared to Atorvastatin, on Glucose Metabolism in Prediabetics with Hypertension and Dyslipidemia: Rationale and Design for the China Hemoglobin A1c Metabolism Protection Union Study (CAMPUS)**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30187345

ABSTRACT

BACKGROUND: Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD). In 2012, over 270 million patients (25.2%) in China were hypertensive and 40.4% was dyslipidemic. The majority of these patients rely on statins for the prevention of cardiovascular disease. However, certain types of statins (e.g., atorvastatin), compared to others (e.g., pitavastatin), may be associated with unfavorable effects on glucose metabolism. This leads to concerns when prescribing statins to patients who also have a predisposition to glucose metabolic disorders (i.e., prediabetes). Thus, this study aims to investigate the effect of

pitavastatin, compared to atorvastatin, on glucose metabolism, as measured by hemoglobin A1c (HbA1c), in Chinese prediabetics with hypertension and dyslipidemias. METHODS: The China hemoglobin A1c Metabolism Protection Union Study (CAMPUS) is a multi-center, prospective, open-label, 12-month, two-arm parallel group, and non-inferiority randomized controlled trial (RCT). A total of 396 prediabetics with hypertension and dyslipidemias will be randomly assigned 1:1 to either pitavastatin 2 mg/day or atorvastatin 20 mg/day, and followed for 12 months (follow-up visits at 1, 3, 6, and 12 months) for HbA1c levels, as well as other measures of glucose metabolism, serum lipid levels, blood pressure control, measures of inflammation, vascular endothelial function, carotid atherosclerosis, and hypertension-related left ventricular hypertrophy. If the results of low-density lipoprotein cholesterol (LDL-C) levels in month 3 after treatment initiation do not meet individual target, drug dose for the participant would be doubled. DISCUSSION: CAMPUS will be the first RCT to investigate the effect of pitavastatin, compared to atorvastatin, on glucose metabolism in Chinese prediabetics with hypertension and dyslipidemias. Further, this study might eventually provide information to design a clinical strategy, and facilitate the improvement of primary prevention in patients at risk for diabetes and CVD. TRIAL REGISTRATION: ClinicalTrials.gov number: NCT03532620. Registered 22 May 2018.

[11] *Ma L, Dai J, Chen J et al.* **Research Progress of Angiogenesis in Atherosclerotic Plaque in Chinese Medicine and Western Medicine**. Chinese journal of integrative medicine 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30178090
ABSTRACT
Angiogenesis in atherosclerotic plaque plays a critical role in the mechanism of atherosclerotic physiopathology. Present consensus shows that angiogenesis in atherosclerotic plaque is mainly resulted in hypoxia, inflammation and some pro-angiogenic factors. The homeostasis in plaque, which is hypoxic and infiltrated by inflammatory cells, may lead to angiogenesis, increase the plaque instability and the incidence rate of vascular events. This article reviews the progression of pathogenetic mechanism, physiopathological significance, relevant detecting technique and corresponding therapeutic methods of Chinese and Western medicine of angiogenesis in atherosclerotic plaque, so as to provide more theoretical basis for atherosclerotic clinical treatment.

[12] *Iqbal R, Akhtar MS, Hassan MQ et al.* **Pitavastatin ameliorates myocardial damage by preventing inflammation and collagen deposition via reduced free radical generation in isoproterenol-induced cardiomyopathy**. Clinical and experimental hypertension (New York, N.Y. : 1993) 2018:1-10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30192645
ABSTRACT
Pitavastatin inhibits 3 hydroxy 3 methyl glutaryl coenzyme A (HMGCoA) reductase enzyme, preventing cholesterol synthesis along with elevating high density apolipoprotein A1 (Apo-A1). The present study was designed to evaluate cardioprotective potential of pitavastatin at 1 mg/kg/day and 3 mg/kg/day dose for 14 days in low dose isoproterenol (ISO) (5 mg/kg/day for 7 consecutive days) induced myocardial damage. ISO administration induced significant reduction in endogenous antioxidant enzymes like reduced glutathione (GSH), superoxide

dismutase (SOD), catalase (CAT) and raised thiobarbituric acid reactive substances (TBARS) indicating activated lipid peroxidation. Along with this, a significant increase in level of cardiac injury biomarkers vie, creatine kinase (CK-MB), lactate dehydrogenase (LDH), aspartate amino transferase (AST), tumor necrosis factor (TNF-alpha) and transforming growth factor (TGF-beta) as well as brain natriuretic peptide (BNP). Histological examination also revealed marked myocardial tissue damage in ISO treated rats. However, pretreatment with pitavastatin (3 mg/kg/day) significantly maintained nearly normal levels of cardiac biomarkers and oxidant antioxidant status as well as lipid peroxidation in ISO induced MI rats. Cardiac histological assessment and infarct size assessment also showed marked reduction in myocardial architecture alteration including infarct size as well as collagen deposition by pitavastatin that strongly supported biochemical findings. These observations strongly corroborate that pitavastatin prevents myocardial damages via up regulation of endogenous oxidants along with its hypocholesterolemic activity.

[13] *Yuan X, Li X, Ji Z et al.* **Effects of vitamin C supplementation on blood pressure and hypertension control in response to ambient temperature changes in patients with essential hypertension**. Clinical and experimental hypertension (New York, N.Y. : 1993) 2018:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30183398
ABSTRACT
Evidence for blood pressure-lowering effects of vitamin C (VC) supplementation in clinical trials is inconsistent and limited studies have examined the effect of VC supplementation on hypertension (HTN) control. In this study, eligible patients were cluster assigned to receive 300 mg VC per day or nothing for 6 months. During the 6-month follow-up period, a questionnaire survey was obtained and standardized blood pressure measurements were performed on all subjects. Oral administration of VC significantly decreased the diastolic blood pressure and pulse pressure with a significant increase in HTN control. After adjusting for confounding variables, treatment with VC was associated with ~ 0.5 risk reduction of uncontrolled HTN in subjects received anti-hypertensive medications, whereas lower indoor and outdoor and ground temperature were significantly associated with an increased risk of uncontrolled HTN in all patients. Our results warrant further studies investigating the mechanisms underlying the association between VC and HTN control.

[14] *Yong WC, Sanguankeo A, Upala S*. **Association between primary Sjogren's syndrome, arterial stiffness, and subclinical atherosclerosis: a systematic review and meta-analysis**. Clinical rheumatology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30178172
ABSTRACT
In rheumatoid arthritis and systemic lupus erythematosus, cardiovascular disease is frequently one of the leading causes of mortality or morbidity. Studies have shown that acute systemic inflammation and chronic systemic vasculitis are associated with endothelial dysfunction and atherosclerotic plaque formation, subsequently leading to cardiovascular disease. This meta-analysis aimed to explore the association of subclinical atherosclerosis and arterial stiffness in primary Sjogren's syndrome. A comprehensive search of the MEDLINE and Embase databases was performed from date of inception through August 2017. The inclusion criterion was

observational studies evaluating the association between primary Sjogren's syndrome, subclinical atherosclerosis, and arterial stiffness by measuring pulse wave velocity (PWV) and intima-media thickness (IMT). Definitions of PSS and methods to assess PWV and IMT were recorded for each study. Different locations of IMT were evaluated including common carotid, internal carotid, and femoral arteries. The pooled mean difference (MD) of PWV and IMT and 95% confidence interval (CI) were calculated using a random-effect meta-analysis. The between-study heterogeneity of effect size was quantified using the Q statistic and I(2). Data were extracted from eight observational studies involving 767 subjects. Pooled result demonstrated a significant increase in PWV in patients who have PSS compared with controls (MD = 1.30 m/s; 95% CI 0.48-2.12; p value = 0.002; I(2) = 85%). Patients with PSS also have higher IMT (MD = 0.08 mm; 95% CI 0.04-0.11; p value < 0.01; I(2) = 72%). Our study suggests that PSS is associated with arterial stiffness and subclinical atherosclerosis. Further studies need to be conducted to find the correlation of subclinical atherosclerosis in PSS with the cardiovascular event, the pathophysiological changes of arterial stiffness in PSS, and the benefit of statins, because controlling cardiovascular risk factors or disease activity could potentially help avoid progression of atherosclerosis to overt cardiovascular disease.

[15] *Shahbaz A, Aziz K, Umair M et al.* **A Patient with Artifactually Low Serum High Density Lipoprotein Cholesterol Due to Waldenstrom Macroglobulinemia**. Cureus 2018; 10:e2900.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30181932

ABSTRACT

When very low or undetectable high density lipoprotein (HDL)-cholesterol (HDL-C) is encountered in clinical practice, a paraproteinemia should be suspected in the absence of genetic or more obvious secondary causes. We reported a case of artifactually low HDL-C in a 68-year-old man with a past medical history of vitamin B12 deficiency. Lipid panel showed total cholesterol (TC) 144 mg/dl, triglycerides (TG) 79 mg/dl, HDL-C 5 mg/dl, and low density lipoprotein (LDL) 123 mg/dl. HDL-C, which was determined three years prior to this presentation was found normal. The patient was prescribed extended release nicotinic acid. Further workup performed showed the ratio of APO B/APO A1 0.36 and direct LDL 28 mg/dl. In the absence of genetic or more obvious secondary causes, we hypothesized that low HDL-C in this patient was due to paraprotein interference in vitro with the liquid homogenous HDL assay. Serum protein electrophoresis demonstrated normal IgG and IgA and an abnormally high IgM at 3510 mg/dl (57-266). A bone marrow biopsy revealed Waldenstrom macroglobulinemia. A diagnostic workup for an isolated low HDL-C unmasking the diagnosis of Waldenstrom macroglobulinemia has been rarely reported. Care must be taken when using the homogeneous method for direct measurement of HDL-C as artifactually undetectable HDL-C might result in the mismanagement of patients with paraproteinemia.

[16] *Madsen MM, Kaersvang L, Hansen AW et al.* **Optimisation of quality indicators for lipid-lowering treatment of type 2 diabetes mellitus**. Danish medical journal 2018; 65.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30187860

ABSTRACT

INTRODUCTION: The Danish Adult Diabetes Database (DADD) annually reports a quality indicator for lipid-lowering treatment of type 2 diabetes mellitus (T2DM) patients. This

retrospective cohort study aims to A) investigate the reasons for inadequate or lacking lipid-lowering treatment and to B) assess the validity of the DADD indicator as a measure of quality of care. METHODS: A) A pop-up questionnaire enquiring about reasons for lack of treatment was added to the clinicians' data entry tool in the Central Denmark Region. B) The DADD indicator was compared on a per-clinic basis with the achieved median low-density lipoprotein (LDL) cholesterol level and with an internationally widely used indicator of lipid-lowering treatment quality. RESULTS: A) A total of 3,491 patients were registered from 1 January 2013 to 28 February 2015. For 170 (62%) of 309 patients with an LDL level > 2.5 mmol/l who were not receiving lipid-lowering treatment, there was no "good" explanation for lacking treatment. Among 518 patients with an LDL level > 2.5 mmol/l despite lipid-lowering treatment, 259 (50%) did not receive high-intensity treatment. B) The DADD quality indicator was neither associated with the international quality indicator nor with the median per-clinic LDL level for T2DM patients. CONCLUSIONS: A) We found substantial potential for improvement of lipid management among T2DM patients in Denmark by initiating and/or intensifying lipid-lowering treatment. B) The current DADD indicator is not a valid measure of lipid-lowering quality of care. FUNDING: supported by the Rosa and Asta Jensen Foundation. TRIAL REGISTRATION: not relevant.

[17] *Leiter LA, Tinahones FJ, Karalis DG et al.* **Alirocumab safety in people with and without diabetes mellitus: pooled data from 14 ODYSSEY trials**. Diabetic medicine : a journal of the British Diabetic Association 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30183102
ABSTRACT
AIM: To evaluate the safety of the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor alirocumab according to diabetes mellitus status. METHODS: Safety data from 14 trials (8-104-week durations) were analysed by treatment (alirocumab or placebo/ezetimibe control) and diabetes status (yes/no, defined by medical history). Adverse event data were assessed using descriptive statistics and Cox models. RESULTS: Of the 5234 trial participants, 1554 (29.7%) had diabetes. Overall, treatment-emergent adverse events were similar in the alirocumab and control groups, except for more frequent local injection site reactions with alirocumab. Fewer people with diabetes experienced local injection site reactions [alirocumab, 3.5%, control, 2.9%; hazard ratio 1.24 (95% CI 0.68-2.25)] than those without diabetes [alirocumab, 7.5%; control, 4.9%; hazard ratio 1.51 (95% CI 1.13-2.01)]. Those with diabetes reported a greater number of serious adverse events (alirocumab, 19.4%; control, 19.7%) than those without diabetes (alirocumab, 14.5%; control, 13.5%). In people with diabetes, major adverse cardiac events occurred in 2.7% of alirocumab-treated people [control, 3.3%; hazard ratio 0.74 (95% CI 0.41-1.35)]; in those without diabetes, 1.8% of alirocumab-treated people had major adverse cardiac events [control, 1.7%; hazard ratio 0.95 (95% CI 0.56-1.62)]. Overall, no increase in HbA1c or fasting plasma glucose vs control treatment groups was observed, regardless of diabetes status. CONCLUSION: This pooled analysis across 14 trials demonstrated similar safety for alirocumab vs control treatment, irrespective of diabetes status, except for more frequent local injection site reactions with alirocumab. People with diabetes reported fewer local injection site reactions than those without diabetes.

[18] *Pereira LC, de Paula ES, Pazin M et al.* **Niacin prevents mitochondrial oxidative stress caused by sub-chronic exposure to methylmercury**. Drug and chemical toxicology 2018:1-7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30192646

ABSTRACT

Humans and animals can be exposed to different chemical forms of mercury (Hg) in the environment. For example, methylmercury (MeHg)-contaminated fish is part of the basic diet of the riparian population in the Brazilian Amazon Basin, which leads to high total blood and plasma Hg levels in people living therein. Hg induces toxic effects mainly through oxidative stress. Different compounds have been used to prevent the damage caused by MeHg-induced reactive oxygen species (ROS). This study aims to investigate the in vivo effects of sub-chronic exposure to low MeHg levels on the mitochondrial oxidative status and to evaluate the niacin protective effect against MeHg-induced oxidative stress. For this purpose, Male Wistar rats were divided into four groups: control group, treated with drinking water on a daily basis; group exposed to MeHg at a dose of 100 microg/kg/day; group that received niacin at a dose of 50 mg/kg/day in drinking water, with drinking water being administered by gavage; group that received niacin at a dose of 50 mg/kg/day in drinking water as well as MeHg at a dose of 100 microg/kg/day. After 12 weeks, the rats, which weighed 500-550 g, were sacrificed, and their liver mitochondria were isolated by standard differential centrifugation. Sub-chronic exposure to MeHg (100 microg/kg/day for 12 weeks) led to mitochondrial swelling ($p < 0.05$) and induced ROS overproduction as determined by increased DFCH oxidation ($p < 0.05$), increased gluthatione oxidation ($p < 0.05$), and reduced protein thiol content ($p < 0.05$). In contrast, niacin supplementation inhibited oxidative stress, which counteracted and minimized the toxic MeHg effects on mitochondria.

[19] *Li X, Sun S, Xu X et al.* **The Association between Genetic Polymorphisms and Simvastatin-Induced Myopathy: A Narrative Synthesis of Evidence**. Drug research 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30193394

ABSTRACT

BACKGROUND AND STUDY AIM: Genetic polymorphisms may play a role in muscular injury associated with simvastatin, but results were inconclusive. This study aimed to summarize evidence from the literature investigating the effects of genetic polymorphism on simvastatin-induced myopathy. METHODS: Studies regarding the association between genetic polymorphisms and simvastatin-induced myopathy were retrieved through electronic databases from February 1, 1990 to March 15, 2018. Two authors independently extracted data, including PMID, author, publication year, country, race, age, population characteristics, drugs, definition of case and control, gene, allele, SNP position, Hardy-Weinberg equilibrium, number of genotypes (case and control), minor allele frequency of cases and controls, association, study type and the Newcastle-Ottawa scale. Due to high heterogeneity in study design and outcome measurements among the included articles, a narrative synthesis of the evidence was conducted. RESULTS: A total of 10 association studies were identified in this study, including SLCO1B1, ABCB1, GATM, HTR3B, HTR7, RYR2 and HLA-DRB1. The evidence linking myopathy to rs4149056 in SLCO1B1 is of high quality, and this association has been reproduced in randomized trials and clinical practice-based cohorts. As for other candidate

genetic markers, the evidences are limited or controversial, and additional well-designed studies with larger sample sizes, are required to further elucidate this association. CONCLUSION: SLCO1B1 genotype is a useful biomarker for predicting an increased risk of simvastatin-induced myopathy.

[20] *Toribio M, Fitch KV, Stone L et al.* **Assessing statin effects on cardiovascular pathways in HIV using a novel proteomics approach: Analysis of data from INTREPID, a randomized controlled trial**. EBioMedicine 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30174281
ABSTRACT
BACKGROUND: People with HIV (PWH) demonstrate increased cardiovascular disease (CVD), due in part to increased immune activation, inflammation, and endothelial dysfunction. METHODS: In a randomized trial (INTREPID), 252 HIV-infected participants with dyslipidemia and no history of coronary artery disease were randomized (1:1) to pitavastatin 4mg vs. pravastatin 40mg for 52weeks. Using a proteomic discovery approach, 92 proteins biomarkers were assessed using Proximity Extension Assay technology to determine the effects of statins on key atherosclerosis and CVD pathways among PWH. 225 participants had specimens available for biomarker analysis pre- and post-baseline. FINDINGS: The mean age was 49.5+/-8.0 (mean+/-SD), LDL-C 155+/-25mg/dl and CD4 count 620+/-243 cell/mm(3). Among all participants, three proteins significantly decreased: tissue factor pathway inhibitor [TFPI; t-statistic=-6.38, FDR p-value<0.0001], paraoxonase 3 [PON3; t-statistic=-4.64, FDR p-value=0.0003], and LDL-receptor [LDLR; t-statistic=-4.45, FDR p-value=0.0004]; and two proteins significantly increased galectin-4 [Gal-4; t-statistic=3.50, FDR p-value=0.01] and insulin-like growth factor binding protein 2 [IGFBP-2; t-statistic=3.21, FDR p-value=0.03]. The change in TFPI was significantly different between the pitavastatin and pravastatin groups. Among all participants, change in TFPI related to the change in LDL-C (r=0.43, P<0.0001) and change in Lp-PLA2 (r=0.29, P<0.0001). INTERPRETATION: Using a proteomics approach, we demonstrated that statins led to a significant reduction in the levels of TFPI, PON3, and LDLR and an increase in Gal-4 and IGFBP-2, key proteins involved in coagulation, redox signaling, oxidative stress, and glucose metabolism. Pitavastatin led to a greater reduction in TFPI than pravastatin. These data highlight potential novel mechanisms of statin effects among PWH. FUND: This work was supported by an investigator-initiated grant to S.K.G. from KOWA Pharmaceuticals America, Inc. and the National Institutes of Health [P30 DK040561; Nutrition Obesity Research Center at Harvard]. M.T. was support by National Institutes of Health [5KL2TR001100-05; Harvard Catalyst KL2 grant].

[21] *Gasparotto J, Chaves PR, da Boit Martinello K et al.* **Obese rats are more vulnerable to inflammation, genotoxicity and oxidative stress induced by coal dust inhalation than non-obese rats**. Ecotoxicology and environmental safety 2018; 165:44-51.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30179764
ABSTRACT
Obesity is an important nutritional disorder worldwide. Its association with environmental pollution may trigger an increase in oxidative stress and inflammatory parameters. Coal is a resource used throughout the world as an important fuel source for generating electricity. The

ashes released by the coal combustion cause serious problems for human health due to their high toxicity and their capacity to bioaccumulate. The aim of this work was to investigate the effects of coal dust inhalation in the organs of obese and non-obese Wistar rats. Pro-inflammatory cytokines, oxidative stress, oxidative damage, histological analysis, comet assay, and micronuclei were investigated. Both obesity and coal dust inhalation increased the pro-inflammatory cytokines IL-1beta and TNF-alpha and decreased HSP70 levels in serum, however, in obese animals that inhaled coal dust these changes were more pronounced. Liver histological analysis showed severe microvesicular steatosis in obese animals that inhaled coal dust. Lung histologic investigation showed abnormalities in lung structure of animals exposed to coal dust and showed severe lung distensibility in obese animals exposed to coal dust. The comet assay showed DNA damage in animals subjected to coal. In addition, there were modulations in enzymatic activities and damage to protein and lipids. Based on our results, the coal dust inhalation can potentiate the pro-inflammatory profile present in obese rats. We also observed an increase in the protein oxidative damage in obese rats that inhaled coal dust. Taken together, our results suggest that the combination of obesity and coal inhalation increased the risks of the development of diseases related to oxidative stress and inflammation.

[22] *Sobhy M, El Etriby A, El Nashar A et al.* **Prevalence of lipid abnormalities and cholesterol target value attainment in Egyptian patients presenting with an acute coronary syndrome**. The Egyptian heart journal : (EHJ) : official bulletin of the Egyptian Society of Cardiology 2018; 70:129-134.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30190636
ABSTRACT
Background: Effective management of hyperlipidemia is of utmost importance for prevention of recurring cardiovascular events after an acute coronary syndrome (ACS). Indeed, guidelines recommend a low-density lipoprotein cholesterol (LDL-C) level of <70mg/dL for such patients. The Dyslipidemia International Study II (DYSIS II) - Egypt was initiated in order to quantify the prevalence and extent of hyperlipidemia in patients presenting with an ACS in Egypt. Methods: In this prospective, observational study, we documented patients presenting with an ACS at either of two participating centers in Egypt between November 2013 and September 2014. Individuals were included if they were over 18years of age, had a full lipid profile available (recorded within 24h of admission), and had either been taking lipid-lowering therapy (LLT) for >/=3months at time of enrollment or had not taken LLT. Data regarding lipid levels and LLT were recorded on admission to hospital and at follow-up 4months later. Results: Of the 199 patients hospitalized for an ACS that were enrolled, 147 were on LLT at admission. Mean LDL-C at admission was 127.1mg/dL, and was not significantly different between users and non-users of LLT. Only 4.0% of patients had an LDL-C level of <70mg/dL, with the median distance to this target being 61.0mg/dL. For the patients with LDL-C information available at both admission and follow-up, LDL-C target attainment rose from 2.8% to 5.6%. Most of the LLT-treated patients received statin monotherapy (98.6% at admission and 97.3% at follow-up), with the mean daily statin dose (normalized to atorvastatin) increasing from admission (30mg/day) to follow-up (42mg/day). Conclusions: DYSIS II revealed alarming LDL-C goal attainment, with none of the patients with follow-up information available reaching the target of LDL-C <70mg/dL, either at hospital admission or 4months after their ACS event. Improvements in guideline

adherence are urgently needed for reducing the burden of cardiovascular disease in Egypt. Strategies include the effective use of statins at high doses, or combination with other agents recommended by guidelines.

[23] *Ozgen Saydam B, Sonmez M, Simsir IY et al.* **A subset of patients with acquired partial lipodystrophy developing severe metabolic abnormalities**. Endocrine research 2018:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30182761
ABSTRACT
Purpose/Aim of the study: Acquired partial lipodystrophy (APL) is a rare disease characterized by selective loss of adipose tissue. In this study, we aimed to present a subset of patients with APL, who developed severe metabolic abnormalities, from our national lipodystrophy registry. MATERIALS AND METHODS: Severe metabolic abnormalities were defined as: poorly controlled diabetes (HbA1c above 7% despite treatment with insulin more than 1 unit/kg/day combined with oral antidiabetics), severe hypertriglyceridemia (triglycerides above 500 mg/dL despite treatment with lipid-lowering drugs), episodes of acute pancreatitis, or severe hepatic involvement (biopsy-proven non-alcoholic steatohepatitis (NASH)). RESULTS: Among 140 patients with all forms of lipodystrophy (28 with APL), we identified 6 APL patients with severe metabolic abnormalities. The geometric mean for age was 37 years (range: 27-50 years; 4 females and 2 males). Five patients had poorly controlled diabetes despite treatment with high-dose insulin combined with oral antidiabetics. Severe hypertriglyceridemia developed in five patients, of those three experienced episodes of acute pancreatitis. Although all six patients had hepatic steatosis at various levels on imaging studies, NASH was proven in two patients on liver biopsy. Our data suggested that APL patients with severe metabolic abnormalities had a more advanced fat loss and longer disease duration. CONCLUSIONS: We suggest that these patients represent a potential subgroup of APL who may benefit from metreleptin or investigational therapies as standard treatment strategies fail to achieve a good metabolic control.

[24] *Mintzer S, Trinka E, Kraemer G et al.* **Impact of carbamazepine, lamotrigine, and levetiracetam on vascular risk markers and lipid-lowering agents in the elderly**. Epilepsia 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30178473
ABSTRACT
OBJECTIVE: To examine serologic markers of vascular risk under treatment with commonly used antiepileptic drugs (AEDs) in the elderly in a randomized setting, and to determine whether the reduced exposure to hydroxymethylglutaryl-CoA reductase inhibitors ("statins") caused by carbamazepine reduces the effectiveness of the drugs as lipid-lowering agents. METHODS: Standard lipid fractions, lipoprotein(a), and C-reactive protein (CRP) were examined in a subset of those participating in the STEP-ONE trial, in which elderly patients with new epilepsy were randomized to treatment with carbamazepine, lamotrigine, or levetiracetam. Separate comparisons were made by individual AED, among those treated with statins, and, for CRP, among those treated with anti-inflammatory drugs. RESULTS: One hundred ninety-four patients had the aforementioned serologic measurements. In patients not taking statins, those treated with carbamazepine had higher total cholesterol than those treated with levetiracetam (+16.6

mg/dL, P = 0.053), with values from patients on lamotrigine intermediate, whereas cholesterol fractions were subject to drug-gender interactions which did not show a consistent pattern. Lipoprotein(a) was significantly lower in lamotrigine patients than in the carbamazepine and levetiracetam groups. After accounting for the effects of steroids, CRP was higher in carbamazepine patients than in other patients. Patients taking a statin had lower lipid levels than those not taking a statin regardless of AED, but the differences between statin-treated and non-statin-treated patients were much larger (50%-100% or more) in the lamotrigine and levetiracetam groups than in the carbamazepine group (P = 0.035 for interaction effect of statin use and AED on total cholesterol). SIGNIFICANCE: Here, we demonstrate that carbamazepine significantly interferes with the ability of statins to lower total cholesterol, thus making it a poor choice for hyperlipidemic patients or those with cardiovascular disease. Native AED effects on lipids were inconsistent and subject to drug-gender interaction, in contrast with other studies; further investigation is necessary to determine if these latter findings are genuine or spurious.

[25] *Guo ZY, Zhang B, Yan YH et al.* **Specific matrix metalloproteinases and calcification factors are associated with the vulnerability of human carotid plaque**. Experimental and therapeutic medicine 2018; 16:2071-2079.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186442
ABSTRACT
The rupture of atherosclerotic plaque provokes the majority of acute cerebrovascular events. Studies have demonstrated that various matrix metalloproteinases (MMPs) may promote atherosclerotic plaque progression and rupture. However, results have been incongruous and the mechanisms of this remain obscured. Therefore, in the current study, carotid plaques were characterized by assessing the levels of MMPs and calcification factors, and evaluating their association with plaque vulnerability. Human carotid plaques were obtained from carotid endarterectomies, and classified into stable and vulnerable groups by ultrasonography and histological analyses. The mRNA and protein levels of MMPs, vascular endothelial growth factor (VEGF), bone sialoprotein 2 (BSP) and osteopontin were investigated by reverse transcription-quantitative polymerase chain reaction and western blotting, respectively. Immunohistochemistry was used to localize MMP-2 and MMP-14 in stable and vulnerable plaques. The activation of various associated signaling pathways was also investigated using western blotting. The mRNA levels of MMP-2, -7, -9 and -14 were elevated in vulnerable plaques, among which expression of MMP-2 and -14 were the highest. Consistent with the mRNA levels, the protein levels of MMP-2 and -14 were also elevated. Immunohistochemistry also demonstrated positive staining of MMP-2 and MMP-14 in vulnerable plaques. Factors that indicate neovascularization and calcification, including VEGF and BSP, were concurrently elevated in vulnerable plaques. In addition, the protein levels of extracellular regulated kinase (ERK) and protein kinase C (PKC) were upregulated in vulnerable plaques. The current study provides novel insights into the MMP profiles of vulnerability plaques, and may assist in the development of novel methods for the diagnosis of plaque vulnerability and the prevention of plaque rupture.

[26] *Lu D, Mai HC, Liang YB et al.* **Beneficial Role of Rosuvastatin in Blood-Brain Barrier Damage Following Experimental Ischemic Stroke**. Frontiers in pharmacology 2018; 9:926.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186167

ABSTRACT

Hemorrhage transformation is the most challenging preventable complication in thrombolytic therapy and is related to recombinant tissue plasminogen activator (rt-PA)-induced blood-brain barrier (BBB) damage. Intraperitoneal injections of normal or high doses of rosuvastatin were administered to Balb/c mice 20 min prior to middle cerebral artery occlusion (MCAO) surgery for 3 h followed by reperfusion with rt-PA thrombolytic therapy and cerebral blood flow monitoring to investigate whether a high or normal dose of rosuvastatin reduces BBB damage after brain ischemia and rt-PA reperfusion. The integrity of the BBB was ameliorated by normal and high doses of rosuvastatin as determined from Evans blue staining, ultrastructure assessments and immunochemistry at 24 h after reperfusion. The levels of TJ proteins were preserved, potentially by targeting platelet-derived growth factor receptor alpha (PDGFR-alpha) and low-density lipoprotein receptor-related protein 1 (LRP1) to inhibit the expression of matrix metalloproteinase proteins (MMPs) by reducing the levels of phosphorylated c-jun-N-terminal kinase (pJNK), phosphorylated mitogen-activated protein kinase (MAPK) p38 (pP38) and increasing the levels of phosphorylated extracellular regulated protein kinases (pERK), and tissue inhibitor of metalloproteinases (TIMPs), as inferred from Western blotting and molecular docking analyses. In summary, rosuvastatin reduced rt-PA therapy-associated BBB permeability by PDGFR-alpha- and LRP1-associated MAPK pathways to reduce the mortality of mice, and a normal dose of rosuvastatin exerted greater preventative effects on reducing BBB damage than did a high dose in the time window of thrombolytic therapy.

[27] *Fremont A, Kim AY, Bailey K et al.* **One In Five Fewer Heart Attacks: Impact, Savings, And Sustainability In San Diego County Collaborative**. Health affairs (Project Hope) 2018; 37:1457-1465.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30179541

ABSTRACT

Before 2011 rates of hospitalization for heart attacks were about the same in San Diego County as they were in the rest of California. In 2011 a multistakeholder population health collaborative consisting of partners at the federal, state, and local levels launched Be There San Diego. The collaborative's goal was to reduce cardiovascular events through the spread of best practices aimed at improving control of hypertension, lipid levels, and blood sugar and through patient and medical community activation. Using hospital discharge data for the period 2007-16, we compared acute myocardial infarction (AMI) hospitalization rates in San Diego County and the rest of the state before and after the demonstration project started. AMI hospitalization rates decreased by 22 percent in San Diego County versus 8 percent in the rest of the state, with an estimated 3,826 AMI hospitalizations avoided and $86 million in savings in San Diego. Results show that a science-based health collaborative can improve outcomes while lowering costs, and efforts are under way to ensure the collaborative's sustainability.

[28] *He W, Huang Y, Zhang Y et al.* **Cardiac rehabilitation therapy for coronary slow flow phenomenon**. Herz 2018.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30191265

ABSTRACT

OBJECTIVE: To evaluate the effectiveness of cardiac rehabilitation on coronary slow flow phenomenon. METHOD: Included were 30 consecutive patients from June 2015 to June 2017. A thrombolysis in myocardial infarction (TIMI) frame evaluation was used to estimate coronary blood flow velocity. All coronary angiography diameters were normal, but blood flow levels did not reach the TIMI level 3. All patients were treated with aspirin and rosuvastatin. Patients were randomly assigned to an experimental group (cardiac rehabilitation treatment group, n= 15) or a control group (normal treatment without cardiac rehabilitation, n= 15). Plasma low density lipoprotein cholesterol (LDL-C), triglyceride (TG), high-sensitivity C reactive protein (hs-CRP), homocysteine (Hcy) and arginine (Arg) expression levels were collected after admission. These indices were reviewed again after 20-30 weeks, improved subjective symptoms were evaluated by multiple outcome criteria (MOCs), and coronary angiography was used to evaluate the velocity of coronary artery blood flow. RESULT: The expression levels of LDL-C and TG in the experimental group were significantly lower than those of the control group (both P< 0.01). The plasma levels of hs-CRP, Hcy and Arg were lower than those in the control group (all P< 0.01). In the experimental group, subjective symptoms of chest pain were significantly improved and the coronary artery blood flow velocity was significantly increased compared with the control group (P< 0.01). CONCLUSION: Cardiac rehabilitation can reduce the plasma levels of LDL-C, TG, hs-CRP, Hcy and Arg, significantly improve the symptoms of coronary slow flow phenomenon and accelerate the speed of coronary artery blood flow.

[29] *Ozdogan AI, Ilarslan YD, Kosemehmetoglu K et al.* **In Vivo Evaluation of Chitosan Based Local Delivery Systems for Atorvastatin in Treatment of Periodontitis**. Int J Pharm 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30194012
ABSTRACT
Periodontitis is a local inflammatory disease initiated by bacteria accumulation and results in cytokine mediated alveolar bone resorption and tissue destruction. In this study, the effect of locally delivered atorvastatin (2% w/v) containing chitosan formulations in the treatment of periodontitis was evaluated in rats with ligature induced periodontitis. The levels of interleukin-1beta (IL-1beta), IL-6, IL-8, IL-10, transforming growth factor-beta1 (TGF-beta1), TGF-beta2 and TGF-beta3 were measured after treatment with formulations. Histomorphometric analysis included the measurements of the area of alveolar bone and the distance between cemento-enamel junction (CEJ) and connective tissue attachment to tooth. Inflammatory and osteoclastic activity scores were given semiquantitatively. Following the administration of atorvastatin, release of pro-inflammatory (IL-1beta, IL-6 and IL-8) and anti-inflammatory (TGF-beta1 and TGF-beta2) cytokines was found to decrease, with a significant alveolar bone healing, when compared to that of control. The anti-inflammatory effect was observed to enhance in presence of chitosan. These findings suggest that chitosan based delivery system for a statin group drug, atorvastatin is a promising for the treatment of periodontal disease.

[30] *Bezek S, Brnoliakova Z, Sotnikova R et al.* **Monotherapy of experimental metabolic syndrome: I. Efficacy and safety**. Interdisciplinary toxicology 2017; 10:81-85.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30174530
ABSTRACT

Literature update week 36 (2018)

Elevated plasma cholesterol, especially low density lipoprotein (LDL) cholesterol, is one of the major risk factors for atherosclerosis and coronary heart disease. Hereditary hypertriglyceridemic rats (hHTG) were developed as a new inbred model for the study of relationships between blood pressure and metabolic abnormalities. The aim of this work was to determine the cholesterol-lowering and antioxidant effects of the novel pyridoindol derivative SMe1EC2, compared to the cholesterol-lowering drug atorvastatin, in rats fed either standard or high-fat and high-cholesterol diet (HFC; 1% cholesterol and 7.5% lard fat). Male hHTG rats fed HFC (HTG+HFC) were administered with SMe1EC2 or atorvastatin (both 50 mg/kg/day p.o.) for 4 weeks. Physiological status of animals was monitored by the measurement of preprandial glucose levels and blood pressure. Lipid profile was characterized by the serum levels of total cholesterol (TC), HDL-, LDL-cholesterol and triglycerides (TRG). The concentration of thiobarbituric acid reactive substances (TBARS) was evaluated in the kidney, liver and serum. Further, the assessment of pro-inflammatory cytokines TNF-alpha, IL-1 and IL-6 in the serum was completed. Feeding the animals with HFC diet resulted in increased serum levels of TC, LDL and TRG. SMe1EC2 ameliorated serum levels of LDL in hHTG rats, both on standard and HFC diet. These effects were comparable with those of the standard hypolipidemicum atorvastatin. SMe1EC2 lowered blood pressure, tissue TBARS concentrations and serum IL-1 levels of HTG+HFC rats. Beneficial effects together with very good toxicity profile predestinate SMe1EC2 to be promising agent for further surveys related to metabolic syndrome features.

[31] *Knezl V, Sotnikova R, Brnoliakova Z et al.* **Monotherapy of experimental metabolic syndrome: II. Study of cardiovascular effects**. Interdisciplinary toxicology 2017; 10:86-92.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30174531

ABSTRACT

Metabolic syndrome belongs to the most important risk factors of cardiovascular diseases. The aim of this study was to investigate changes in cardiovascular system induced by high cholesterol and high fat diet (HCHF) in HTG rats and their influence by a pyridoindole antioxidant - SMe1EC2 (S). The effects of S were compared with those of atorvastatin (A). Male HTG rats were fed HCHF (1% cholesterol + 7.5% lard) for 4 weeks. S and A were administered p.o., 50 mg/kg b.w. Following experimental groups were used: Wistar rats (W), hypertriglyceridemic rats (HTG), HTG rats fed HCHF (CHOL), HTG+S (S-HTG), CHOL+S (S-CHOL), and CHOL+A (A-CHOL). Values of blood pressure (BP) and selected ECG parameters were monitored in conscious animals, functions of the isolated heart and aorta were analyzed ex vivo. At the end of the experiment, systolic (sBP) and diastolic (dBP) blood pressure was increased in HTG and CHOL. S and A decreased BP in all treated groups. Accordingly with BP changes, the aortic endothelial function of CHOL was damaged. Both S and A administration ameliorated the endothelium-dependent relaxation to values of W. PQ and QTc intervals were prolonged in CHOL, while the treatment with S or A improved ECG findings. Prodysrhythmogenic threshold was decreased significantly in CHOL and both treatments returned it to the control values. In conclusion, HCHF increased BP, impaired endothelial relaxation of the aorta and potentiated susceptibility of myocardium to dysrhythmias. The effect of S on the changes induced by HCHF diet was more pronounced than that of A.

[32] *Foroughinia F, Jamshidi E, Javanmardi H et al.* **Effectiveness and safety of omega-3 fatty acids for the prevention of ischemic complications following carotid artery stenting: An early terminated pilot study**. Iranian journal of neurology 2018; 17:11-17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186554

ABSTRACT
Background: We aimed to study the possible beneficial effects of omega-3 polyunsaturated fatty acids (PUFAs) in carotid artery stenting (CAS) procedure for decreasing post-procedural ischemic complications. Although previous evidence demonstrated that omega-3 PUFAs, present in fish oil, can significantly enhance platelet response to antiplatelet agents after percutaneous coronary intervention (PCI), it is unknown whether they can be used in patients undergoing CAS. Methods: The single-blind, case-control, pilot randomized trial study was planned to perform on 60 patients undergoing CAS (30 in case and 30 in control group). Patients in both groups were pretreated with dual antiplatelet therapy (aspirin 80 mg/day with a loading dose of 325 mg, and clopidogrel 75 mg/day after a loading dose of 600 mg) at least 48 hours before the CAS. 30 patients randomly received 3000 mg loading dose of omega-3 fatty acids 12 hours before the procedure and 1000 mg omega-3 capsule the day after the procedure. All subjects were planned to be visited by neurologist for any peri- and post-procedural complications immediately after the procedure and on first, seventh, and thirtieth days. Results: We ended the study after the enrollment of 18 patients because of an unexpected hemorrhagic transformation in case group. Two patients in this group developed hemorrhagic symptoms less than 12 hours after the procedure. One of the failures occurred in a patient with small vessel disease. Except these two cases, no one showed any neurological deficit symptoms in both groups. Conclusion: In patients already receiving dual antiplatelet treatment before CAS, adding omega-3 PUFAs would increase the incidence of hemorrhagic transformation.

[33] *Wan Dali WPE, Jan Mohamed HJ, Yusoff H*. **Nutrient Intakes Status and Physical Inactivity among Overweight and Obese School Children in Kota Bharu, Kelantan, Malaysia**. Iranian journal of public health 2018; 47:1098-1107.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186781

ABSTRACT
Background: The study examined the baseline findings of a controlled intervention study comprising anthropometric measurements, nutrient intakes, and physical activity among overweight or obese children in Kota Bharu, Kelantan, Malaysia. Methods: The study was completed in 2016 and the baseline data were gathered from four groups in a school-based randomized community trial among Year Five students from primary schools in Kota Bharu, Kelantan, Malaysia. Participants completed anthropometry assessment, three-day dietary record, and Physical Activity Questionnaire for Older Children (PAQ-C). Results: The prevalence of obesity was higher among the boys (52.5%). Mean energy intake was significantly higher among boys as compared to the girls (P=0.003). Twenty-five percent of the participants had exceeded the recommended nutrient intakes (RNI) of energy recommended. The calcium, thiamine, riboflavin, and niacin were also significantly higher among boys as compared to the girls (P<0.05). Boys also exhibited a significantly higher score on performance of physical activity (mean=2.68; SD=0.60) as compared to the girls (mean=2.38; SD=0.51) however it is still

in the category of moderately active. Approximately 14.4% of children had a very low physical activity level. Conclusion: Overweight and obese boys had higher energy and fat intakes but were more physically active as compared to the girls. These findings might be useful in planning appropriate intervention strategies to be designed and delivered especially for this cohort.

[34] *Han Y, Guan M, Zhu Z et al.* **Assessment of longitudinal distribution of subclinical atherosclerosis in femoral arteries by three-dimensional cardiovascular magnetic resonance vessel wall imaging**. Journal of cardiovascular magnetic resonance : official journal of the Society for Cardiovascular Magnetic Resonance 2018; 20:60.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30173671

ABSTRACT

BACKGROUND: Lower extremity peripheral artery disease has become a significant health burden worldwide. Since the treatment strategies can be different if atherosclerotic disease involves different femoral artery segments, it is important to assess plaque distribution among different segments of femoral arteries. We sought to investigate the longitudinal distribution of subclinical femoral artery atherosclerosis in asymptomatic elderly adults using cardiovascular magnetic resonance (CMR) vessel wall imaging. METHODS: Asymptomatic elderly subjects underwent three-dimensional (3D) CMR vessel wall imaging for femoral arteries. The 3D motion sensitized-driven equilibrium prepared rapid gradient-echo (3D-MERGE) sequence was acquired from the common femoral artery to the popliteal artery. The femoral artery was divided into 4 segments: common femoral artery (CFA), proximal superficial femoral artery (pSFA), adductor canal (AC) segment of femoral artery, and popliteal artery (PA). The morphological characteristics including lumen area, wall area, maximum and minimum wall thickness, normalized wall index (NWI = wall area / [lumen area + wall area] x 100%), and eccentricity index ([maximum wall thickness - minimum wall thickness] / maximum wall thickness), luminal stenosis, and presence of atherosclerotic plaque were evaluated and compared between bilateral sides and among different femoral artery segments in each side of femoral artery. The associations between ankle-brachial index (ABI) and cardiovascular risk factors and femoral artery plaque characteristics were also determined. RESULTS: Of 107 recruited subjects (71.9 +/- 5.6 years; 48 males), 70 (65.4%) were found to have femoral artery plaques. The atherosclerotic plaques were most frequently found in PA (41.1%) and CFA (40.2%) segments, followed by pSFA (31.8%) and AC (23.4%) segments ($p = 0.002$). Similarly, PA and CFA segments showed significantly greater maximum wall thickness and eccentricity index compared with pSFA and AC segments (all $p < 0.001$). Significant differences can be found in NWI among four segments of femoral arteries ($p < 0.001$) and PA showed the highest NWI (54.8%), followed by AC (54.3%), pSFA (52.4%) and CFA (45.9%) segments. Compared with right femoral artery, left femoral artery had significant smaller lumen area and greater NWI in most of segments ($p < 0.002$). There were no significant differences in ABI between subjects with and without atherosclerotic plaques ($p = 0.161$). The presence of subclinical atherosclerotic plaque in femoral arteries was significantly associated with cardiovascular risk factors including age (odds ratio [OR], 1.133; 95% confidence interval [CI], 1.048-1.224, $p = 0.002$), male gender (OR, 3.914; 95% CI, 1.612-9.501, $p = 0.003$), and hypertension (OR, 4.000; 95% CI, 1.700-9.411, $p = 0.001$), respectively. CONCLUSIONS: Subclinical femoral artery atherosclerosis is prevalent in the elderly population, particularly in the left femoral artery and segments of CFA and PA, and is

associated with age, male gender and hypertension. Our findings suggest that, for screening subclinical atherosclerosis, more attention needs to be paid to the specific side and segments of femoral arteries, particularly older individuals and those with these cardiovascular disease risk factors.

[35] *Koohestanimobarhan S, Salami S, Imeni V et al.* **Lipophilic statins antagonistically alter the major epithelial-to-mesenchymal transition signaling pathways in breast cancer stem-like cells via inhibition of the mevalonate pathway**. Journal of cellular biochemistry 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30191610
ABSTRACT
Resistance to therapies, recurrence, and metastasis remain challenging issues for breast cancer patients, particularly for triple-negative and breast cancer stem cells. The activation of the epithelial-to-mesenchymal transition (EMT) plays an indispensable role in the poor prognosis of those types. The accumulating proofs indicated that the mevalonate pathway crucially mediates a poor prognosis. Here, the effects of lipophilic 3-hydroxy-3-methyl-glutaryl-coenzyme A inhibitors, atorvastatin, lovastatin, and simvastatin, were investigated on expression and function of a selected profile of EMT-related genes in breast cancer stem-like cells. A nontoxic dose of statins (5 muM for 4 days) significantly ($P < 0.05$ and >2-fold change) altered expression of 50 of 71 studied genes with a shared cluster of 37 genes that are coding chief operator of signaling pathways in Hippo, Notch, Wnt, proliferation, invasion, angiogenesis, and cell death. They also significantly decreased the levels of Yap/Taz proteins and shifted the expression of vimentin/E-cadherin in favor of induction of differentiation. Statins significantly chemosensitized the treated cells to doxorubicin and also reduced in vitro migration of the cells. Whereas lovastatin and simvastatin significantly decreased the expression of CD44, atorvastatin drastically increased CD24 and caused more wide-ranging impacts. In summary, the statins hold back the process of EMT by the antagonizing of EMT-promoting pathways. High degree of overlapping findings is supportive of the central role of the mevalonate pathway in cancer stem-like cells, but further studies are required to find the optimized chemical structure for the maximum abrogation of orchestrated EMT pathways.

[36] *Bahammam MA, Attia MS*. **Effects of Systemic Simvastatin on the Concentrations of Visfatin, Tumor Necrosis Factor-alpha, and Interleukin-6 in Gingival Crevicular Fluid in Patients with Type 2 Diabetes and Chronic Periodontitis**. Journal of immunology research 2018; 2018:8481735.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186882
ABSTRACT
Purpose: The objective of this study is to explore the relationship between the levels of interleukin- (IL-) 6, tumor necrosis factor- (TNF-) alpha, and visfatin and simvastatin usage, in the gingival crevicular fluids (GCFs) of diabetic patients afflicted with chronic periodontitis. Methods: Eighty outpatients at the Periodontology Department, Faculty of Dentistry, University Dental Hospital (King Abdulaziz University), were categorized into 4 groups (20 patients per group), on the basis of radiological evaluation of bone loss, clinical attachment levels (CAL), probing depth (PD), and gingival indices: group 1 (healthy periodontium), group 2 (chronic periodontitis + type 2 diabetes), group 3 (chronic periodontitis), and group 4 (type 2 diabetes +

chronic periodontitis + simvastatin). Enzyme-linked immunosorbent assays were used to measure IL-6, TNF-alpha, and visfatin levels. Results: Significantly elevated levels of IL-6, TNF-alpha, and visfatin were seen in group 2 in comparison to groups 1 and 3. Reduced levels were seen in group 4 due to simvastatin usage. Positive association was seen between periodontal variables and the levels of IL-6, TNF-alpha, and visfatin. Conclusion: Periodontal destruction and diabetes have a synergistic effect on the elevation of inflammatory cytokine levels. Simvastatin may be beneficial in improving periodontal health among diabetic patients.

[37] *Gayam V, Mandal AK, Gill A et al.* **A Rare Case of Acute Pancreatitis Due to Very Severe Hypertriglyceridemia (>10 000 mg/dL) Successfully Resolved With Insulin Therapy Alone: A Case Report and Literature Review**. Journal of investigative medicine high impact case reports 2018; 6:2324709618798399.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186885
ABSTRACT
A 48-year-old male presented to the psychiatric emergency room for dysmorphic mood. He was admitted to medical service for the management of hyponatremia, which was discovered in his initial laboratory workup. After the first day of admission, he developed abdominal pain and fever, and subsequent laboratory work revealed a triglyceride level of 10 612 mg/dL (reference range = 0-194 mg/dL). Computed tomography scan of the abdomen and pelvis revealed a hypodense lesion in the pancreas surrounded by a moderate amount of peripancreatic fluid suggestive of hemorrhagic pancreatitis. Based on the laboratory findings and imaging, we diagnosed acute pancreatitis (AP) secondary to hypertriglyceridemia. The patient was initiated on intravenous fluids and insulin to help decrease the triglyceride level with the plan to initiate apheresis. However, the patient improved on insulin therapy alone, which negated the need for apheresis, and the patient was discharged with fenofibrate with no further complications. While elevated triglycerides are a well-known cause of AP, we sought to assess various treatment options in management, especially considering a severely elevated triglyceride level of >10 000 mg/dL. Along with supportive care in AP, there are additional options in hypertriglyceridemia AP, including heparin, insulin, apheresis, antioxidants, and fibrates. Currently, there are no clear guidelines favoring one therapeutic option over the other.

[38] *Bianconi S, Santillan ME, Solis MDR et al.* **Effects of dietary omega-3 PUFAs on growth and development: Somatic, neurobiological and reproductive functions in a murine model**. The Journal of nutritional biochemistry 2018; 61:82-90.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30189366
ABSTRACT
Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) are relevant to fetal and infant growth and development. OBJECTIVE: to assess whether long-term exposure to dietary omega-3 PUFA imbalance alters pre- and/or postnatal pups' development and reproductive function later in life. Mice dams were fed with omega-3 PUFA Control (soybean oil, 7%), Deficient (sunflower oil, 7%) or Excess (blend oil; 4.2% cod-liver+2.8% soybean) diet before conception and throughout gestation-lactation and later on, their pups received the same diet from weaning to adulthood. Offspring somatic, neurobiological and reproductive parameters were evaluated. Excess pups were lighter during the preweaning period and shorter in length from postnatal day (PND) 7 to

49, compared to Control pups (P<.05). On PND14, the percentage of pups with eye opening in Excess group was lower than those from Control and Deficient groups (P<.05). In Excess female offspring, puberty onset (vaginal opening and first estrus) occurred significantly later and the percentage of parthenogenetic oocytes on PND63 was higher than Control and Deficient ones (P<.05). Deficient pups were shorter in length (males: on PND14, 21, 35 and 49; females: on PND14, 21 and 42) compared with Control pups (P<.05). Deficient offspring exhibited higher percentage of bending spermatozoa compared to Control and Excess offspring (P<.05). These results show that either an excessively high or insufficient omega-3 PUFA consumption prior to conception until adulthood seems inadvisable because of the potential risks of short-term adverse effects on growth and development of the progeny or long-lasting effects on their reproductive maturation and function.

[39] *Zhou J, Tang L, Shen CL, Wang JS*. **Green tea polyphenols modify gut-microbiota dependent metabolisms of energy, bile constituents and micronutrients in female Sprague-Dawley rats**. The Journal of nutritional biochemistry 2018; 61:68-81.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30189365
ABSTRACT
Our recent metagenomics analysis has uncovered remarkable modifying effects of green tea polyphenols (GTP) on gut-microbiota community structure and energy conversion related gene orthologs in rats. How these genomic changes could further influence host health is still unclear. In this work, the alterations of gut-microbiota dependent metabolites were studied in the GTP-treated rats. Six groups of female SD rats (n=12/group) were administered drinking water containing 0%, 0.5%, and 1.5% GTP (wt/vol). Their gut contents were collected at 3 and 6 months and were analyzed via high performance liquid chromatography (HPLC) and gas chromatography (GC)-mass spectrometry (MS). GC-MS based metabolomics analysis captured 2668 feature, and 57 metabolites were imputatively from top 200 differential features identified via NIST fragmentation database. A group of key metabolites were quantitated using standard calibration methods. Compared with control, the elevated components in the GTP-treated groups include niacin (8.61-fold), 3-phenyllactic acid (2.20-fold), galactose (3.13-fold), mannose (2.05-fold), pentadecanoic acid (2.15-fold), lactic acid (2.70-fold), and proline (2.15-fold); the reduced components include cholesterol (0.29-fold), cholic acid (0.62-fold), deoxycholic acid (0.41-fold), trehalose (0.14-fold), glucose (0.46-fold), fructose (0.12-fold), and alanine (0.61-fold). These results were in line with the genomic alterations of gut-microbiome previously discovered by metagenomics analysis. The alterations of these metabolites suggested the reduction of calorific carbohydrates, elevation of vitamin production, decreases of bile constituents, and modified metabolic pattern of amino acids in the GTP-treated animals. Changes in gut-microbiota associated metabolism may be a major contributor to the anti-obesity function of GTP.

[40] *Zawacki A, Dodge A, Eickhoff J et al.* **Novel Lipid Thresholds for Screening Predict the Need for Pharmacotherapy**. J Pediatr 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30172432
ABSTRACT

OBJECTIVE: To identify non-high-density lipoprotein cholesterol (HDL-C) and HDL-C thresholds for pediatric nonfasting lipid screens that are more predictive of the need for lipid-lowering pharmacotherapy and estimate numbers of potentially avoidable fasting lipid panels. STUDY DESIGN: In this retrospective review of children and youths aged 8-21 years presenting for preventive cardiology care, initial lipid results, recommendations for pharmacotherapy, and presence of additional cardiovascular risk factors were noted. Receiver operating characteristic curve analysis calculated threshold lipid values predicting the need for pharmacotherapy and were applied to 2 screening populations. Rates of potentially unnecessary fasting lipid panels were calculated. RESULTS: A non-HDL-C value >156 mg/dL for children with >/=1 cardiovascular risk factors and >199 mg/dL for children without risk factors conferred 95% or greater sensitivity in predicting a recommendation for pharmacotherapy with higher specificity, positive predictive value, and negative predictive value compared with current guidelines. HDL-C was a poor predictor of pharmacotherapy. Application of the current thresholds to screening populations indicated that 38.5%-92.3% of follow-up fasting lipid panels would not result in pharmacotherapy. CONCLUSION: Using higher non-HDL-C and lower HDL-C thresholds could prevent unnecessary follow-up lipid panels and reduce patient anxiety, cost, and time. This could improve compliance with universal pediatric lipid screening for both health care providers and families.

[41] *Mor LT, Holley K*. **A Case Report of Anticoagulation Management in Acquired Hemophilia Associated With Levofloxacin**. Journal of pharmacy practice 2018:897190018799186.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30189787
ABSTRACT
PURPOSE: To report a case of acquired hemophilia secondary to levofloxacin and provide a guide for the use of anticoagulation in acute coronary syndrome. CASE SUMMARY: A 75-year-old female treated with levofloxacin presented with spontaneous bruising of the upper extremities. Levofloxacin was discontinued and the symptoms resolved. Thereafter, the spontaneous bruising recurred and progressed over a few weeks. The patient was treated with recombinant factor VIIA with a time to recuperation of 3 months. The patient was subsequently found to have ST-segment elevation for which they received unfractionated heparin, ticagrelor, and aspirin prior to bare metal stent placement. CONCLUSION: Hemophilia A is a rare disease associated with high morbidity and mortality. Case studies previously evaluating the association of levofloxacin with acquired hemophilia have shown causality. Initiating anticoagulation in patients with acquired hemophilia has long been a challenge to clinicians as evidence-based guidelines are lacking and bleeding risk may outweigh the benefit of anticoagulation. Furthermore, factor VIII deficiency does not provide additive protection against atherosclerotic plaque formation. This case report supports existing literature associating levofloxacin with acquired hemophilia. Due to the complication of life-threatening bleeds, familiarity with the treatment course following coronary events will allow patients with acquired hemophilia to be adequately and safely anticoagulated.

[42] *Banik S, Hossain MS, Bhatta R, Akter M*. **Attenuation of lipid peroxidation and atherogenic factors in diabetic patients treated with gliclazide and metformin**. Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences 2018; 23:77.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30181759

ABSTRACT

Background: Diabetes is associated with oxidative stress and considered as a major risk factor for cardiac disease. We attempted to investigate the role of oral antidiabetic (OAD) agents gliclazide and metformin in lowering the lipid peroxidation and managing the risk for cardiovascular (CV) complications in diabetic patients in comparison with nondiabetic healthy individuals. Materials and Methods: This cross-sectional study was comprised of 150 individuals grouped in three, namely, Group A (n = 60) healthy volunteers, Group B (n = 30) newly diagnosed diabetes, and Group C (n = 60) diabetes treated with OAD. Serum malondialdehyde (MDA), nitric oxide (NO), and Vitamin C were assessed for studying lipid peroxidation status, whereas serum triglyceride (TG) and total cholesterol were monitored as predictors for CV risk. Results: We found significantly higher concentrations of MDA and NO levels ($P < 0.001$) in both groups of patients (Group B and C) in comparison to control group (Group A). Regarding antioxidants, significantly lower concentrations of Vitamin C ($P = 0.046$) were found in Group B and C compared to Group A. Moreover, there was significant difference exhibited in concentration level of MDA ($P = 0.001$) and NO ($P = 0.015$) between Group B and C, whereas difference of Vitamin C ($P = 0.147$) was not statistically significant. Conclusion: Our data confirmed that treatment with gliclazide and metformin significantly reduced the lipid peroxidation accompanied with attenuated levels of serum TGs and cholesterol and suggested that oral hypoglycemic agents have great impact to reduce the oxidative stress and increase the antioxidant status in diabetes.

[43] *Roopmani P, Krishnan UM*. **Harnessing the pleiotropic effects of atorvastatin-fenofibrate combination for cardiovascular stents**. Materials science & engineering. C, Materials for biological applications 2018; 92:875-891.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30184817

ABSTRACT

Atorvastatin and fenofibrate have been conventionally employed as lipid-lowering agents. They also exhibit beneficial effects in the treatment of endothelial dysfunction, oxidative stress and vascular inflammation due to their pleiotropic effects that include vasodilatory and anti-inflammatory effects. These pleiotropic effects may serve to overcome the drawbacks of late stent thrombosis and delayed endothelialization that plague conventional drug eluting stents. However, the combination has not been explored yet as therapeutic coatings in drug eluting stents. The present study aims to investigate the potential of atorvastatin-fenofibrate combination loaded in a biodegradable poly(l-lactide-co-caprolactone) polymer film to inhibit thrombus formation and macrophage activation apart from exploring their effect on the proliferation of smooth muscle cells and endothelial cells. The dual drug-loaded polymer films were characterized by spectroscopy and calorimetry. In vitro studies revealed that the combination effectively retarded the proliferation of only smooth muscle cells but not the endothelial cells which augers well for stent applications where rapid re-endothelialization is preferred. Further, the dual drug-loaded films exhibited a marked decrease in the adhesion and activation of platelets and macrophages revealing the potent anti-thrombogenic and anti-inflammatory effects of the combination. The pleiotropic effects of the combination may be

attributed to their ability to activate nitric oxide synthase in endothelial cells while mTOR levels remained unaltered by the combination.

[44] *Sun B, Rui R, Pan H et al.* **Effect of Combined Use of Astragaloside IV (AsIV) and Atorvastatin (AV) on Expression of PPAR-gamma and Inflammation-Associated Cytokines in Atherosclerosis Rats**. Medical science monitor : international medical journal of experimental and clinical research 2018; 24:6229-6236.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30190450
ABSTRACT
BACKGROUND The aim of this study was to assess the effect of combined use of Astragaloside IV(AsIV) and atorvastatin (AV) on the expression of PPAR-gamma and inflammation-associated cytokines in atherosclerosis rats. MATERIAL AND METHODS High-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) in plasma were detected through automatic biochemical analyzer and the histopathological analysis was performed via HE staining. The levels of oxidized low-density lipoprotein (oxLDL) and tumor necrosis factor-alpha (TNF-alpha), and interleukins (IL)-6 and IL-18 in serum were detected by ELISA. The expressions of proliferator-activated receptor-gamma (PPAR-gamma), cluster of differentiation 36 (CD36), matrix metalloprotein-9 (MMP-9), intercellular cell adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1(VCAM-1), and p38 and P-p38 levels were detected by Western blot. RT-PCR was used to detect the mRNA expressions of nuclear factor-kappaB (NF-kappaB), PPAR-gamma, CD36, MMP-9, ICAM-1, and VCAM-1. RESULTS Administration of AsIV and AV significantly decreased the lipid content and oxLDL in plasma. The levels of TNF-alpha, IL-6, and IL-18 were significantly decreased in AsIV, AV, and AsIV + AV groups, especially in the AsIV + AV group. Administration decreased the levels of NF-kappaB, CD36, MMP-9, ICAM-1, VCAM-1, and P-p38 expression and increased the expression of peroxisome PPAR-gamma. Compared with the NC group, the atherosclerotic lesions significantly increased in the HD group, while the combined administration significantly inhibited the development of atherosclerotic disease. CONCLUSIONS Combined administration of AV and AsIV showed potent effects against atherosclerosis through the NF-kappaB/PPARgamma pathway, which may be a new therapy for treatment of atherosclerosis in the future.

[45] *Mirzapour H, Panahi HA, Moniri E, Feizbakhsh A*. **Magnetic nanoparticles modified with organic dendrimers containing methyl methacrylate and ethylene diamine for the microextraction of rosuvastatin**. Mikrochimica acta 2018; 185:440.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30173349
ABSTRACT
Magnetic nanoparticles (MNPs) modified with organic dendrimers are shown to be a viable sorbent of the microextraction of the drug rosuvastatin (RST; also known as Crestor). The MNPs were prepared from iron(II) chloride and iron(III) chloride and then coated with silicon dioxide. The coated MNPs produced by this method have diameters ranging from 10 to 60 nm according to scanning electron microscopy. The MNPs were further modified with organic dendrimers containing methyl methacrylate and ethylene diamine. The resulting MNPs were characterized by SEM, Fourier transform infra-red and thermal gravimetry analysis. Then, the efficacy of the

modified MNPs with respect to the extraction of RST was studied. The adsorption of RST by MNPs can be best described by a Langmuir isotherm. Following elution with buffer, RST was quantified by HPLC. The method was applied to the determination of RST in (spiked) human blood plasma, urine, and in tablets. RST extraction efficiencies are 54.5% in plasma, 86.6% from the drug matrix, and 94.3% in urine. The highest adsorption capacity of the RST by the MNPs adsorbent was 61 mgg(-1). Graphical abstract Co-precipitation was used to synthesize magnetic nanoparticles (MNPs). They were coated with a layer of SiO2 and then branched by organic dendrimers containing methyl methacrylate (MMA) and ethylene diamine (EDA). Rosuvastatin (RST) drug was trapped between dendrimer branches, therefore adsorption capacity of the drug was strongly increased.

[46] **Bezafibrate in Primary Biliary Cholangitis**. The New England journal of medicine 2018; 379:984-985.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30184460
ABSTRACT

[47] *Huang X, Wu X, Yan S, Lan T*. **[Lipid-lowering effect of propolis in mice with Triton-WR1339-induced hyperlipidemia and its mechanism for regulating lipid metabolism]**. Nan fang yi ke da xue xue bao = Journal of Southern Medical University 2018; 38:1020-1024.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30187881
ABSTRACT
OBJECTIVE: To evaluate the therapeutic effect of propolis against Triton-WR1339-induced hyperlipidemia in mice and explore the underlying mechanism. METHODS: C57BL/6 mice were randomly divided into 7 groups (n=10), including the control group, hyperlipidemia model group, fenofibrate (30 mg/kg) treatment group, and 4 treatment groups treated with low- (30 mg/kg) or high-dose (60 mg/kg) propolis HB01 or HB02. In all but the control group, acute hyperlipidemia models were established by intramuscular injection of Triton WR-1339, and corresponding treatments were administered via gastric lavage for 7 days. After the treatments, blood samples were collected for testing the levels of total cholesterol (TC), triglycerides (TG), highdensity lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), malondialdehyde (MDA), superoxide dismutase (SOD), alanine aminotransferase (GPT), and aspartate aminotransferase (GOT); Western blotting was used to detect the expressions of the proteins involved in lipid metabolism in the liver tissues including ABCA1, ABCG8, LDLR, and SR-B1. RESULTS: Compared with the normal control group, the mice with Triton-WR1339-induced hyperlipidemia showed significantly increased levels of TC, TG, LDL, MDA, GPT, and GOT and lowered HDL-C levels and SOD activity ($P < 0.05$). Treatments with fenofibrate and the 2 propolis at either low or high dose significantly reversed Triton-WR1339-induced changes in blood lipids ($P < 0.05$), and the effects of propolis were more potent. Triton-WR1339 injection also significantly decreased the expressions levels of ABCA1, ABCG8, LDLR, and SR-B1 in the liver ($P < 0.05$), and these changes were obviously reversed by treatments with fenofibrate and propolis ($P < 0.05$), especially by the latter. CONCLUSIONS: The lipid-lowering effects of propolis are mediated by improving lipid metabolism and regulating the expressions of lipid transport proteins in the liver tissue.

Literature update week 36 (2018)

[48] *Jiang S, Li S, Hu J et al.* **Combined delivery of angiopoietin-1 gene and simvastatin mediated by anti-intercellular adhesion molecule-1 antibody-conjugated ternary nanoparticles for acute lung injury therapy**. Nanomedicine : nanotechnology, biology, and medicine 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30193816
ABSTRACT
Effective treatment for acute lung injury (ALI) is in high demand. Lung-targeted ternary nanoparticles containing anti-intercellular adhesion molecule-1 (ICAM-1) antibody-conjugated simvastatin-loaded nanostructured lipid carrier (ICAM/NLC), protamine (Pro), and angiopoietin-1 (Ang-1) gene (ICAM-NLC/Pro/Ang) were developed for ALI therapy. The ternary nanoparticles with different weight ratios of ICAM-NLC to Ang-1 gene were prepared via charge interaction. The anti-ICAM-1 antibody-conjugated ternary nanoparticles exhibited higher cellular uptake and transfection efficiency (from 26.7% to 30.9%) in human vascular endothelial cell line EAhy926 than the non-targeted control. The largest size of ICAM-NLC/Pro/Ang (357.1nm) was employed for further study, which significantly up-regulated in vitro and in vivo Ang-1 protein expression. In vivo i.v. administration of ICAM-NLC/Pro/Ang (357.1nm) significantly attenuated pulmonary TNF-alpha and IL-6 levels, inflammatory cell infiltration, and led to positive histological improvements in lipopolysaccharide-induced ALI mice. Collectively, the ICAM-NLC/Pro/Ang that co-delivered simvastatin and Ang-1 gene may represent a potential treatment modality for ALI.

[49] *Zhou F, Rao F, Deng YQ et al.* **Atorvastatin ameliorates the contractile dysfunction of the aorta induced by organ culture**. Naunyn-Schmiedeberg's archives of pharmacology 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30182188
ABSTRACT
Statins are widely used in the treatment of hypercholesterolemia. Studies have demonstrated that statins could maintain vascular contractile function through inhibiting the transformation of vascular smooth muscle cells (VSMCs) from the contractile phenotype to the synthetic phenotype. However, the underlying mechanisms have not been fully elucidated. The effect of atorvastatin on the thoracic aorta of Sprague-Dawley rats cultured in serum-free conditions in vitro was evaluated. Aortic constriction was induced by high potassium, phenylephrine, and CaCl2. The protein expression levels of alpha1 adrenoceptor; inositol 1,4,5-trisphosphate (IP3) receptor; protein kinase Cdelta (PKCdelta); stromal interaction molecule 1 (STIM1); high-voltage activated dihydropyridine-sensitive (L type, Cav1.2) channels; and two contractile phenotype marker proteins [alpha-smooth muscle actin (alpha-SMA) and myosin (SM-MHC)] were determined by western blotting. Compared with the fresh control, the constriction of rat aorta was impaired after culture in serum-free medium for 24 h. The impaired contraction of cultured aortas was mediated by Cav1.2 and store-operated Ca(2+) (SOC) channel, which could be improved by atorvastatin at 20 muM. The protein expression levels of alpha1 adrenoceptor, IP3 receptor, PKCdelta, STIM1, Cav1.2, alpha-SMA, and SM-MHC in the aortas cultured in serum-free conditions were decreased significantly. Atorvastatin partially prevented the reduction in the contractility and the downregulation of these proteins in cultured aortas. The transformation of the VSMC phenotype is associated with the vasoconstriction dysfunction of

cultured aortas. Atorvastatin may protect vascular function by modulating calcium signaling pathways.

[50] *Idzerda NMA, Pena MJ, Parving HH et al.* **Proteinuria and cholesterol reduction are independently associated with less renal function decline in statin-treated patients; apost hoc analysis of the PLANET trials**. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30184238
ABSTRACT
Background: Statins have shown multiple effects on different renal risk factors such as lowering of total cholesterol (TC) and lowering of urine protein:creatinine ratio (UPCR). We assessed whether these effects of statins vary between individuals, the extent of discordance of treatment effects on both TC and UPCR within an individual, and the association of responses in TC and UPCR with estimated glomerular filtration rate (eGFR) decline. Methods: The PLANET I and II (Renal effects of Rosuvastatin and Atorvastatin in Patients Who Have Progressive Renal Disease) trials examined effects of atorvastatin and rosuvastatin on proteinuria and renal function in patients with proteinuria. We post hoc analysed 471 therapy-adherent proteinuric patients from the two trials and assessed the individual variability in UPCR and TC response from 0 to 14 weeks and whether these responses were predictive of eGFR decline during the subsequent 9 months of follow-up. Results: UPCR and TC response varied between individuals: mean UPCR response was -1.3% (5th-95th percentile -59.9 to 141.8) and mean TC response was -93.9 mg/dL (-169.1 to -26.9). Out of 471 patients, 123 (26.1%) showed a response in UPCR but not in TC, and 96 (20.4%) showed a response in TC but not in UPCR. eGFR (mL/min/1.73 m2) did not decrease significantly from baseline in both UPCR responders [0.4; 95% confidence interval (CI) -1.6 to 0.9; P = 0.54] and TC responders (0.3; 95% CI -1.8 to 1.1; P = 0.64), whereas UPCR and TC non-responders showed a significant decline in eGFR from baseline (1.8; 95% CI 0.6-3.0; P = 0.004 and 1.7; 95% CI 0.5-2.9; P = 0.007, respectively). A lack of response in both parameters resulted in the fastest rate of eGFR decline (2.1; 95% CI 0.5-3.7; P = 0.01). These findings were not different for rosuvastatin or atorvastatin. Conclusions: Statin-induced changes in cholesterol and proteinuria vary between individuals and do not run in parallel within an individual. The initial fall in cholesterol and proteinuria is independently associated with a reduction in eGFR decline. This highlights the importance of monitoring both cholesterol and proteinuria after initiating statin therapy.

[51] *de Paula Nascimento-Castro C, Wink AC, da Fonseca VS et al.* **Antidepressant Effects of Probucol on Early-Symptomatic YAC128 Transgenic Mice for Huntington's Disease**. Neural plasticity 2018; 2018:4056383.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30186318
ABSTRACT
Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder caused by a trinucleotide expansion in the HD gene, resulting in an extended polyglutamine tract in the protein huntingtin. HD is traditionally viewed as a movement disorder, but cognitive and neuropsychiatric symptoms also contribute to the clinical presentation. Depression is one of the most common psychiatric disturbances in HD, present even before manifestation of motor

symptoms. Diagnosis and treatment of depression in HD-affected individuals are essential aspects of clinical management in this population, especially owing to the high risk of suicide. This study investigated whether chronic administration of the antioxidant probucol improved motor and affective symptoms as well as hippocampal neurogenic function in the YAC128 transgenic mouse model of HD during the early- to mild-symptomatic stages of disease progression. The motor performance and affective symptoms were monitored using well-validated behavioral tests in YAC128 mice and age-matched wild-type littermates at 2, 4, and 6 months of age, after 1, 3, or 5 months of treatment with probucol (30 mg/kg/day via water supplementation, starting on postnatal day 30). Endogenous markers were used to assess the effect of probucol on cell proliferation (Ki-67 and proliferation cell nuclear antigen (PCNA)) and neuronal differentiation (doublecortin (DCX)) in the hippocampal dentate gyrus (DG). Chronic treatment with probucol reduced the occurrence of depressive-like behaviors in early- and mild-symptomatic YAC128 mice. Functional improvements were not accompanied by increased progenitor cell proliferation and neuronal differentiation. Our findings provide evidence that administration of probucol may be of clinical benefit in the management of early- to mild-symptomatic HD.

[52] *Nakamura M*. **[Evidence Based Secondary Prevention of Ischemic Heart Disease. Topics: I. Advances and Evidence of Pharmacotherapy: 2. Up to Date Lipid Lowering Treatment]**. Nihon Naika Gakkai Zasshi 2017; 106:208-215.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30182645
ABSTRACT

[53] *Al-Ghannami SS, Al-Adawi S, Ghebremeskel K et al.* **Randomized open-label trial of docosahexaenoic acid-enriched fish oil and fish meal on cognitive and behavioral functioning in Omani children**. Nutrition 2018; 57:167-172.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30195244
ABSTRACT
OBJECTIVE: This study aimed to examine the effect of docosahexaenoic acid (DHA)-enriched fish oil supplement and meal of grilled meal on cognitive and behavioral functioning manifested as attention-deficit/hyperactivity disorder in primary school students 9 to 10 y are in Muscat, Oman. METHODS: This randomized open-label trial involved two types of interventions: fish oil supplement or one serving (100 g) of grilled fish per day (Sunday through Friday) for 12 weeks. Red cell total lipid DHA levels were assessed. The Verbal Fluency Test, Buschke Selective Reminding Test, and Trail Making Test were used to measure cognitive functioning. Behavioral functioning was assessed using a standardized Arabic version of the National Initiative for Children's Health Quality Vanderbilt Assessment Scales. All measurements were carried out before and after intervention. RESULTS: DHA levels increased by 72% and 64% in the fish oil (mean, 3.6%-6.2%) and fish-meal (mean, 3.4%-5.6%) groups, respectively (P = 0.000). The Trail Making Test was the only cognitive test that demonstrated marked differences between groups: Median interquartile range difference between pre- and postintervention in the Trail Making Part B score was 61.5 (SE, 19.3, 103.2) in the fish oil versus fish-meal group, 24.5 (SE, -15.2, 74.7, P = 0.005). The Vanderbilt Assessment Scales also showed significant differences between groups (P <0.001). CONCLUSION: This study contributed to available evidence on the

cognitive and behavioral benefits of DHA in healthy school children. Expanding the food fortification program with DHA-enriched fish oil should be considered as part of broader policy to improve child health.

[54] *Sami A, Iftekhar MF, Rauf MA, Sher A*. **Subclinical Hypothyroidism among local adult obese population**. Pak J Med Sci 2018; 34:980-983.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30190765
ABSTRACT
Objective: To determine the frequency of subclinical hypothyroidism in local adult obese population. Methods: The study was conducted at Hayatabad Medical Complex, Peshawar, from March, 2017 to August, 2017. All patients aged between 18 and 60 years with BMI of more than 29kg/m(2) were included in the study. Patients on lipid lowering drugs, with renal failure, hepatic failure and already diagnosed cases of thyroid dysfunction were excluded from the study. Thyroid functions were measured for all patients. Results: A total of 127 adults were included in the study in a consecutive manner. Mean age was 34.5 + 7.9 years of which 46.5% were male and 53.5% were female. Mean BMI was 32.05+/-2.06 kg/m(2). The mean serum TSH was 3.13+/-1.10 mIU/L and mean serum thyroxine level was 1.08+/-0.25ng/dl. Subclinical hypothyroidism was recorded in 15% of the study population. Conclusion: Subclinical hypothyroidism is highly prevalent in our population with BMI of more than 29kg/m(2). Further studies are recommended on relationship between thyroid functions and BMI and its effect on cardiovascular functions.

[55] *Spinu M, Olinic DM, Olinic M, Homorodean C*. **In vivo imaging of complicated atherosclerotic plaque - role of optical coherence tomography (OCT)**. Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie 2018; 59:469-478.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30173250
ABSTRACT
Cardiovascular diseases are the main cause of death worldwide, with coronary artery disease (CAD) being the predominant underlying etiology. Coronary angiography (CA) is the current invasive method used for CAD diagnosis, as well as for defining the coronary interventional treatment strategy. However, CA offers sometimes-poor accuracy in estimating atherosclerotic plaque volume, morphology and degree of stenosis severity. Optical coherence tomography (OCT) is an intracoronary imaging technique, developed in order to overcome CA limitations and is considered to be an "optical biopsy" that provides in vivo imaging. OCT has an extremely high resolution, similar to that of a usual histological evaluation of a biopsy sample. One of the most important clinical research areas for OCT is represented by the study of the pathophysiology of coronary and carotid atherosclerotic disease, in order to improve diagnosis and optimize therapy. This article reviews OCT basic technical aspects related to its diagnosis efficacy, OCT morphological information offered in coronary artery disease, including acute coronary syndromes and non-atherosclerotic coronary disease, OCT use for morphological percutaneous coronary intervention (PCI) follow-up and stent-failure mechanisms, as well as the new three-dimensional (3D)-OCT approach for atherosclerotic plaque assessment.

[56] *Yao GT, Song LP, Xue WH et al.* **Nano-particle engineered atorvastatin delivery to support mesenchymal stem cell survival in infarcted myocardium**. Saudi journal of biological sciences 2018; 25:1016-1021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30174496
ABSTRACT
Atorvastatin (ATV) may support mesenchymal stem cells (MSC) survival in post-infarct myocardium (MI) as inflammatory reactions, oxidative stress and hypoxia condition get started in such tissues after damage. However, limited aqueous insolubility and rapid first-pass metabolism reduce the systemic availability of ATV. The aim of the present investigation was to develop ATV loaded nanoparticles (ATVNPs) which might ensure the maximum availability of ATV in systemic circulation for longer duration and to strengthen the support to MSC survival. ATVNPs were synthesized using double emulsion solvent evaporation method and characterized as spherical shape, positive charged, nanoparticles of uniform size distribution and higher entrapment efficiency. ATVNPs were non-cytotoxic and showed sustained release (up to 28 days). Assessment of cardiac function (in terms of echocardiographic and left heart catheterization parameters) and cytokines estimation revealed efficient improvement in post-infarct myocardium condition of rat. In conclusion, ATVNP was developed successfully that may ensure safe, cost effective, and efficacious treatment of post-infarct myo-cardium when compared with that of MSC alone and MSC supplemented with ATV solution.

[57] *Bolat MS, Bakirtas M, Firat F et al.* **The effect of atorvastatin on penile intracavernosal pressure and cavernosal morphology in normocholesterolemic rats**. Turkish journal of urology 2018:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30183612
ABSTRACT
OBJECTIVE: A debate is open on the effects of lipid-lowering drugs on sexual function. We aimed to investigate the effect of atorvastatin use on penile intracavernosal pressure (ICP) and cavernosal morphology. MATERIAL AND METHODS: Fourteen mature male Sprague-Dawley-rats were randomly assigned to either the control group (which received standard food and water ad libitum) or the atorvastatin group (which received standard food, water, and statin) for twelwe weeks. At the end of the study, ICPs were measured with cavernosometry. Penectomy specimens were histologically examined. RESULTS: The following mean values were obtained for the control and atorvastatin groups, respectively: pre-study body weights (350+/-16.9 g and 331.4+/-24.9 g); post-study body weights (356+/-18 g and 368+/-22.5 g (p>0.05); ICPs at 5 V (5.96+/-5.16 mmHg and 2.11+/-1.22 mmHg (p=0.07)); ICPs at 10 V (18.28+/-14.1 mmHg and 5.56+/-5.58 mmHg) (p=0.09); testosterone (1.23+/-0.78 and 0.78+/-0.58 mmol/dL) (p=0.39); blood glucose (151+/-22 mg/dL and 168.6+/-16.2 mg/dL) (p=0.12); triglyceride (93.4+/-19.8 mg/dL and 52.1+/-18.6 mg/dL) (p=0.01); total cholesterol (50.2+/-7.2 mg/dL and 47.7+/-6.6 mg/dL) (p=0.51); and low-density lipoprotein (LDL) cholesterol (10.0+/-4.4 mg/dL and 3.5+/-2.1 mg/dL) (p=0.01). The mean collagen thickness was similar (p=0.09); but the mean elastin thickness increased in the atorvastatin group (p=0.01). CONCLUSION: The present study showed that the use of atorvastatin reduced the intracavernosal pressure in 10 V stimulation, and minimally decreased testosterone levels in rats, within a short period of time. When statin treatment is considered for its protective properties on cardiovascular system or for its lipid-

lowering effect. It should be kept in mind that atorvastatin may also adversely contribute to erectile dysfunction.

[58] *Tahta A, Izgi N, Bagci-Onder T et al.* **Assessment of the MRI and Behavioral Test Results in a Focal Cerebral Ischemia-Reperfusion Model in the Rat after Separate and Combined Use of Mouse-Derived Neural Progenitor Cells, Human-Derived Neural Progenitor Cells and Atorvastatin**. Turkish neurosurgery 2018; 28:571-581.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30192361
ABSTRACT
AIM: To assess the efficacy of Neural progenitor cell (NPC) transplantation in ischemic stroke, and to investigate whether atorvastatin enhances therapeutic potency of NPC after stroke. MATERIAL AND METHODS: The focal cerebral ischemia-reperfusion model was performed by transient occlusion of middle cerebral artery. Rats were assigned randomly to receive intracerebral transplantation of mouse NPC alone (mNPC), human NPC alone (hNPC), mouse NPC plus oral atorvastatin (mNPC+A), human NPC plus oral atorvastatin (hNPC+A), oral atorvastatin alone, or intracerebral Dulbecco"s Modified Eagle"s medium injection (control group). Adhesive removal, rotarod, cylinder tests, and magnetic resonance imaging (MRI) were used for assessment of rats during 4 weeks. After sacrification on 28th day, rats were investigated by immunofluorescent staining. RESULTS: The hNPC and mNPC groups showed significantly improved functional outcome and reduced infarct area ratio compared with the control group. The hNPC group had significantly better performance and lower infarct area ratio than the mNPC group. Addition of atorvastatin to stem cell therapy significantly improved functional outcome, although it did not affect the infarct area ratio on MRI. Anti-inflammatory response in the infarct area was higher in the mNPC group. NPC transplantation significantly reduced the amount of microglia and a significant increase in the amount of astrocytes. CD8a+ T lymphocyte and granzyme B activities were not detected in any of the subjects. CONCLUSION: Both hNPC and mNPC treatments significantly improved functional outcome, and reduced infarct area ratio after stroke. Atorvastatin enhanced the therapeutic potency of NPCs, including neurological improvement.

[59] *Chiu HT, Shen LJ, Chen YC et al.* **Effect of statin use on the risk of medically attended acute respiratory illness among influenza vaccinated elderly**. Vaccine 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30174239
ABSTRACT
OBJECTIVES: The immunomodulatory effects of statins may reduce the immune response induced by influenza vaccines. However, evidence regarding the effect of statin use on the effectiveness of seasonal influenza vaccines against medically attended acute respiratory illness (MAARI) in the elderly remains scarce. METHODS: We conducted a retrospective cohort study using data from Taiwan's National Health Insurance Research Database. Elderly adults aged>==66years who were vaccinated with seasonal influenza vaccines during the 2007-2008 to 2012-2013 influenza seasons were enrolled for this analysis. We compared the risk of MAARI between statin and non-statin users. Propensity score matching and conditional logistic regression models were used to analyze the data. RESULTS: A total of 440,180 elderly were included in this study. In general, the risk of MAARI was higher in statin users than non-statin

users (odds ratio [OR]: 1.03, 95% confidence interval [CI]: 1.02-1.05). Statin exposure after vaccination was associated with a higher risk of MAARI (OR: 1.05, 95% CI: 1.02-1.07). Among different statin agents, simvastatin and lovastatin use was associated with a significant increase in the risk of MAARI (ORsimvastatin: 1.14, 95% CI: 1.10-1.18; ORlovastatin: 1.18, 95% CI: 1.12-1.25). CONCLUSIONS: Statin exposure, especially simvastatin and lovastatin, was associated with a higher risk of MAARI in the seasonal influenza vaccinated elderly. Future studies exploring the differences between individual statins and mechanisms of their immunomodulatory effects are necessary.

[60] *Gitt AK, Rieber J, Hambrecht R et al.* **Do acute coronary events affect lipid management and cholesterol goal attainment in Germany? : Results from the Dyslipidemia International study II**. Wien Klin Wochenschr 2018.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30178071
ABSTRACT
OBJECTIVE: To document utilization of lipid-lowering therapy, attainment of low-density lipoprotein cholesterol target values, and cardiovascular outcomes in patients hospitalized for acute coronary syndrome in Germany. METHODS: The Dyslipidemia International Study II was a multicenter, observational study of the prevalence of dyslipidemia and lipid target value attainment in patients surviving any acute coronary syndrome event. Among patients on lipid-lowering therapy for >/=3 months, use of lipid-lowering therapy and lipid profiles were assessed at admission and again at 120+/- 15 days after admission (the follow-up time point). Multivariate logistic regression was used to identify variables predictive of low-density lipoprotein cholesterol target value attainment in patients using lipid-lowering therapy. RESULTS: A total of 461 patients hospitalized for acute coronary syndrome were identified, 270 (58.6%) of whom were on lipid-lowering therapy at admission. Among patients on lipid-lowering therapy, 90.7% and 85.9% were receiving statin monotherapy at admission and follow-up, respectively. Mean (SD) low-density lipoprotein cholesterol levels in patients on lipid-lowering therapy were 101 (40) mg/dl and 95 (30) mg/dl at admission and follow-up, respectively. In patients with data at both admission and follow-up (n= 61), low-density lipoprotein cholesterol target value attainment rates were the same (19.7%) at both time points. Smoking was associated with a 77% lower likelihood of attaining the low-density lipoprotein cholesterol target value. CONCLUSION: Hospitalization for an acute event does not greatly alter lipid management in acute coronary syndrome patients in Germany. Both lipid-lowering therapy doses and rates of low-density lipoprotein cholesterol target value attainment remained essentially the same several months after the event.

[61] *Cui B, Sun XW, Zhu YF et al.* **[Relationship between Angiotensin Converting Enzyme Gene Polymorphism and Carotid Atherosclerotic Plaque: A Study Based on Vessel Wall Magnetic Resonance Imaging]**. Zhongguo yi xue ke xue yuan xue bao. Acta Academiae Medicinae Sinicae 2018; 40:493-500.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=30193603
ABSTRACT
Objective To investigate the relationship between angiotensin converting enzyme(ACE) gene polymorphism and carotid plaque composition,vessel wall morphology,and clinical symptoms

based on vessel wall magnetic resonance imaging. Methods Totally 75 hypertensive patients(75 internal carotid artery plaques) with maximum plaque thickness>/=1.5 mm,according to the ACE insertion(I) or deletion(D) gene polymorphism,were divided into ACE 2 genotype group(n=37) and ACE ID/DD genotype group(n=38). The influences of plaque composition,vessel wall morphology,clinical symptoms,and use of ACE inhibitor or angiotensin receptor blocker(ACEI/ARB) on vessel wall morphology were analyzed. Results Compared with ACE 2 genotype group,the ACE ID/DD genotype group had significantly higher incidence of ischemic stroke(Chi(2)=3.921,P=0.048). The plaque composition and vessel wall morphology showed no significant difference between these two groups. Inside ACE ID/DD genotype group,the carotid remodeling index was significantly lower in users of ACEI/ARB than non-users of ACEI/ARB(1.85+/-0.60 vs. 2.48+/-0.40;t=3.854,P=0.001).Conclusion In primary hypertension,ACE ID/DD genotype may be associated with carotid atherosclerotic plaque.