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CARDIOVASCULAR MODULATION OF DIETARY SODIUM RESTRICTION AND β_2 -ADRENERGIC RECEPTOR POLYMORPHISM IN HUMANS. L.H. Eisenach, D.R. Schroeder, T.L. Pike, C.P. Johnson, W.G. Schrage, E.M. Snyder, B.D. Johnson, S.T. Turner, M.J. Joyner, Mayo Clinic College of Medicine, Rochester, MN.

Dietary sodium intake has been shown to influence β_2 -adrenergic receptor (β_2 -AR) responsiveness, and the Gly allele of the Arg16/Gly β_2 -AR polymorphism has been associated with hypertension in a linkage analysis in Rochester, MN. We have also shown that Gly homozygotes (GG) have greater forearm β_2 -AR mediated vasodilation than Arg (AA) after a controlled Na⁺ diet (150 mmol • day⁻¹), and the difference is mediated by endothelial NO. The purpose of this study was to test the hypothesis that dietary Na⁺ restriction affects forearm and systemic β_2 -mediated dilation in healthy nonmotensive humans GG ($n = 17$) vs AA ($n = 15$). We measured HR, MAP, and CO (acetylene breathing) responses to intravenous infusion of terbutaline (TRB) before and after 5 days of dietary Na⁺ restriction (10 mmol • day⁻¹). Also following the diet, a brachial artery catheter was placed to measure forearm blood flow (FBF; plethysmography) responses to isoproterenol (ISO) before and after NO inhibition with L-NMMA. There was a main effect of diet ($p < .03$) on weight loss, increased urine volume, and 24-hour urinary excretion of Na⁺ but no influence from genotype. Diet significantly decreased baseline CO in GG (pre- vs postdiet mean \pm SD: 6.4 ± 1.4 to 5.5 ± 1.2 L • min⁻¹; $p = .003$) but not in AA (5.8 ± 1.3 to 5.6 ± 1.0 L • min⁻¹, NS) and increased peripheral resistance in GG ($p = .02$) but not AA. Baseline HR, MAP, and stroke volume were similar between groups, and the responses of all cardiovascular measures to TRB were not influenced by genotype or diet. In contrast to previous findings after a normal Na⁺ diet, the FBF dose response curves to ISO were not different based on genotype ($p = .51$). L-NMMA decreased baseline FBF and significantly blunted the response to ISO, but there was no evidence to suggest that the responses were influenced by genotype ($p = .89$, genotype-by-ISO-by-L-NMMA interaction). We conclude that dietary Na⁺ restriction negates the increased forearm NO-mediated, β_2 -AR responsiveness in GG subjects, which may explain the diet-evoked baseline increase in peripheral resistance and decrease in CO in this group, providing evidence that Na⁺ intake modulates cardiovascular indices based on the Arg16/Gly β_2 -AR polymorphism.

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SURGICAL TREATMENT OF PERIPHERAL ENTRAPMENT NEUROPATHY OF THE LOWER EXTREMITIES: OUTCOMES FROM 158 CONSECUTIVE SURGICAL CASES.

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Objective: We report the outcome of 158 patients with peripheral entrapment neuropathy treated surgically by multiple nerve decompressions of the peroneal and tibial system. This is a promising approach for the treatment of pain, numbness, and balance disturbance in diabetic and nondiabetic patients with peripheral nerve entrapment syndromes in the lower extremities. **Methods:** Records of 158 consecutive patients with diabetic and nondiabetic neuropathy, treated surgically by multiple nerve decompression, were reviewed to document changes in the visual analogue scale, sensation improvement, reduction in pain medication requirement, and balance improvement. All patients underwent tarsal tunnel release and neurolysis of lower extremity nerves of the tibial and peroneal system as a concomitant part of the procedure. Patients offered surgical intervention met specific criteria including documented sensory abnormalities using neurosensory testing by the Pressure-Specified Sensory Device (PSSD) and a positive Tinel's sign on examination over the involved nerve. **Results:** Eighty-eight percent of the patients with preoperative numbness reported sensation improvement. Eighty-one percent of patients with balance disturbance reported improved balance after the procedure. From those patients who underwent the procedure mainly for pain relief, 83% reported an improvement in the visual analogue scale of more than 50% and 77% improved in more than 5 points of the scale. After the procedure, patients reported a decrease in their pain medication requirement ($p \leq .001$), sensation improvement ($p \leq .001$), and pain relief ($p \leq .001$). **Conclusion:** Similar to experiences found in the upper extremity, nerve decompression in the lower extremity is a safe and effective procedure to improve the quality of life of patients with peripheral neuropathy secondary to nerve compression. Documentation and staging of the severity of neuropathy with neurosensory testing and the presence of Tinel's sign facilitate successful selection of surgical candidates. Decompression and neurolysis of compressed lower extremity nerves are associated with statistically significant improvement in the visual analogue scale and sensation. The great majority of patients are very satisfied with the results.

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ACUTE LUNG INJURY IN THE PEDIATRIC EMERGENCY DEPARTMENT: A

RETROSPECTIVE EVALUATION OF RISK FACTORS FOR INTUBATION. R.J. Freishtat,^{1,2,3} D. Mathison,⁴ J.M. Chamberlain,¹ ¹Division of Emergency Medicine, Children's National Medical Center, Washington, DC; ²Research Center for Genetic Medicine, Children's National Medical Center, Washington, DC; ³School of Medicine and Health Sciences, George Washington University, Washington, DC; ⁴Department of Pediatrics, Northwestern University, Chicago, IL.

Purpose: Early identification of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) is hypothesized to contribute to avoidance of invasive ventilation modalities. There are no studies evaluating ALI in the emergency department (ED), where early identification and interventions are most likely to take place. We aimed to describe the epidemiology of ALI in the ED and to determine factors associated with endotracheal intubation within 24 hours of presentation. **Methods:** Secondary analyses of 11,664 patient records from a study of quality involving 16 EDs were performed. Records were selected if SaO₂ was recorded during the visit. The methods of Ellis and Sevringhaus were used to convert SaO₂ to virtual PaO₂ and allowed calculation of PaO₂:FIO₂ (PF) ratios. Combining these and historical data, patients were classified as having ALI alone, ALI and ARDS, or neither according to 1994 American-European Consensus Conference criteria. **Results:** SaO₂ was recorded in 2,217 patients; 108 (4%) met ALI criteria, including 25 (1%) with ARDS. Logistic regression for all patients showed the following independent associations with ALI: lower SaO₂ (adjusted OR [95 CI] = 2.4 [2.1, 2.8]), lower temperature (4.1 [2.9,6]), and higher PRISA II (1.13 [1.09, 1.18]) (all $p < .001$, $R^2 = .22$, goodness of fit $p > .99$). No association was noted for age, gender, SIRS, shock, pCO₂, CNS, renal or hematologic dysfunction. Twelve (11%) ALI patients were intubated within 24 hours of presentation. Logistic regression for ALI patients showed an independent association for intubation with higher PRISA II only

(1.21 [1.05, 1.39], $p = .007$) ($R^2 = .26$, goodness of fit $p = .36$). **Conclusions:** We found a moderate incidence of nonintubated ALI in the ED. The low R^2 values for the ALI and intubation regression models underscore the lack of criteria for early identification of patients with respiratory compromise. Therefore, the nonintubated ALI patients represent an important group for future studies aimed at early identification of critical illness in the ED.

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T-HELPER 2 LYMPHOCYTE-EXPRESSED NKG2A SUPPRESSES INTERLEUKIN-4 SECRETION UPON CD3/CD28/HLA-E COSTIMULATION: A NOVEL MECHANISM FOR T-HELPER 2 DOMINANCE IN ASTHMA. R.J. Freishtat,^{1,2,3} B. Mojgani,^{2,4} E.P. Hoffman,^{2,3}

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Purpose: Asthma exacerbations are frequently associated with viral infections. Many of these viruses cause a marked decrease in antigen-presenting cell MHC class I production. We have previously identified a potential mechanism linking the T-helper type 2 (T_H2) cytokine preponderance seen in acute asthma and this viral-mediated event. That is, NKG2A was identified as the only known ligand for MHC class I (ie, HLA-E) expressed by activated T_H2 lymphocytes. Therefore, we aimed to measure T_H2 cell effector function upon T cell receptor (TCR) stimulation in the presence and absence of HLA-E, intending to imitate the reduction in MHC class I seen with respiratory viral infections. **Methods:** Human monocytes and T_H2 cells were negatively purified from healthy volunteers using previously validated antibody cocktails. T_H2 cells were cultured in media containing anti-CD3 and anti-CD28 in the presence (or absence) of autologous monocytes, which served as HLA-E presenters. Four-color flow cytometry was performed. Analyses with FlowJo 5.7 were carried out after back-gating on CD3⁺CD4⁺ cells. Paired *t*-tests measured statistical significance using SPSS 14. **Results:** T_H2 isolates were > 95% pure CD3⁺CD4⁺CD8⁻ cells and > 84% pure T_H2 cells. Monocyte isolates were > 90% pure. Flow studies of activated T_H2 cells showed mean \pm SE (mean fluorescence intensity) NKG2A⁺ of $11.4 \pm 0\%$ (15.4 ± 0.1) and intracellular IL-4⁺ of $4.4 \pm 0\%$ (15.3 ± 0.1). In the presence of monocytic HLA-E, activated T_H2 lymphocytes showed NKG2A⁺ of $11.2 \pm 0\%$ (35.6 ± 0) ($p < .001$) and intracellular IL-4⁺ of $0.04 \pm 0.01\%$ (14.1 ± 0) ($p < .001$). There was no detectable switching from inhibitory NKG2A to the activating lectin NKG2C in any sample. **Conclusions:** We identified significant suppression of IL-4 expression in activated T_H2 cells via NKG2A-HLA-E (MHC class I) binding and ultimate TCR signaling inhibition. Extrapolated to a viral-induced asthma exacerbation scenario, where MHC class I and thus HLA-E are in low abundance, we have shown that T_H2 cells would exhibit a relatively robust response. This represents a new aspect of T_H1/T_H2 balance in the inflammatory response and could be clinically important in viral-induced T_H1/T_H2-associated diseases like asthma.

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THE PREVALENCE OF NEUROPSYCHIATRIC SYMPTOMS IN MILD COGNITIVE IMPAIRMENT: A POPULATION-BASED STUDY. Y.E. Geda, W.A. Rocca,* D.S. Knopman,* R. Roberts,* R.C. Petersen,* Mayo Clinic College of Medicine, Jacksonville, FL; *Mayo Clinic College of Medicine, Rochester, MN.

Objective: To estimate the prevalence of neuropsychiatric symptoms among subjects with mild cognitive impairment (MCI) in a defined population. **Background:** The population-based prevalence of neuropsychiatric symptoms in MCI is unknown except for a recent report (Lyketsos et al, 2002, JAMA) that has not yet been replicated. **Design/Methods:** The Mayo Clinic Study of Aging is an NIH-funded population-based study that was launched in October 2004. It is designed to estimate the prevalence and incidence of MCI. Elderly individuals of age 70 to 89 years are being recruited by using a stratified random sampling from the target population of Olmsted County, Minnesota (equal allocation of men and women). All participants undergo neurological, neuropsychiatric, and psychometric evaluations. A consensus panel of behavioral neurologists, geriatrician, neuropsychiatrist, neuropsychologists, and nurses determined the classification of normal cognitive aging, MCI, or dementia based on standard definitions. The Neuropsychiatric Inventory (NPI) was administered to all participants, and the prevalence of symptoms in MCI cases was compared to cognitively normal individuals (controls), matched by age and gender (1 case to 3 controls), by using chi-square or Fisher's exact test. **Results:** Neuropsychiatric data were available on 104 participants with MCI and 312 cognitively normal individuals. The prevalence of apathy was 24% in MCI ($n = 25/104$) vs 6.1% (19/312) in cognitively normal individuals ($p < .0001$). Similarly, there were significant differences in the prevalence of depression 26% vs 11.5% ($p = .0004$), anxiety 11.5% vs 3.9% ($p = .004$), and irritability 18.3% vs 8.7% ($p = .007$). **Conclusions:** The prevalence of neuropsychiatric symptoms in our study is comparable to the published report (Lyketsos et al, 2002) that used a similar design (population based) and measurement instrument (NPI); however, we report a slightly higher frequency of apathy and depression. One major finding of our study is that apathy may be the most distinguishing neuropsychiatric feature between MCI and normal cognitive aging, and this, in turn, may have an implication for a future interventional study that can target apathy in order to delay the progression of MCI to dementia.

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EFFICACY OF CYCLOOXYGENASE 2 INHIBITORS ON TUMOR ANOREXIA-CACHEXIA SYNDROME IN PATIENTS WITH CANCER OF THE HEAD AND NECK AND GASTROINTESTINAL TRACT. V. Lai,³ J. George,³ L. Richey,³ T. Cannon,¹ H.J. Kim,² C. Shores,¹ M. Couch,¹ ¹Departments of ¹Otolaryngology/Head and Neck Surgery (OHNS) and ²General Surgery, and the ³Doris Duke Fellowship Program, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) may palliate cachexia by maintaining muscle mass. A recent animal study demonstrated that cyclooxygenase 2 inhibitors (COX-2) reversed tumor-induced wasting in mice bearing human head and neck squamous cell carcinoma and colon carcinomas. Our hypothesis was that NSAIDs given to patients with cancer cachexia will stabilize or reverse their loss of lean body mass. **Methods:** A prospective, randomized, double-blind, placebo-controlled clinical trial was designed to determine whether intervention with the COX-2 inhibitor celecoxib was effective at improving cancer cachexia in patients with cancer of the head and neck and gastrointestinal (GI) tract. After the clinical diagnosis of cachexia was established, the following measurements were made: weight; body composition via dual x-ray absorptiometry; resting energy expenditure (REE) via indirect calorimetry; quality of life (QoL) surveys via Func-

tional Assessment of Anorexia/Cachexia Therapy (FAACT); and performance status via Karnofsky Performance Scale (KPS). Patients were randomized to receive either celecoxib 200 mg po bid or placebo for 3 weeks. Three weeks later, each patient returned for the same evaluation as on day 1. In this pilot study, no nutritional intervention was made. **Results:** Eleven patients have completed the study thus far. Seven have received placebo, while four have received active drug. Eight patients have head and neck cancers and three patients have cancer of the GI tract. All were male, with a mean age of 59.1 years. Interim unblinded analysis of the data reveals that, on average, patients taking celecoxib experienced weight gain of 1.0 kg (SE = 1.33), body mass index (BMI) increase of 0.31 (SE = 0.45), lean body mass percent (LBM%) increase of 0.28 (SE = 2.81), and improvement of FAACT score of 10 points (SE = 4). Those taking placebo experienced, on average, weight loss of 1.0 kg (SE = 1.63), BMI decrease of 0.56 (0.68), LBM% drop of 0.04% (SE = 1.60), and no improvement in FAACT score. **Conclusions:** Promising initial trends were seen in the administration of celecoxib to patients with cancer cachexia in this study, including gains in weight, BMI, LBM%, and QoL score. Future studies may examine cytokine and CRP levels and may include a nutritional intervention in studying the effect of anti-inflammatory therapy on cancer cachexia.

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AMAUIROSIS FUGAX CAUSED BY THROMBOPHILIA-HYPOFIBRINOLYSIS IN CASES WITHOUT CAROTID ATHEROSCLEROSIS: THERAPY WITH COUMADIN-LOVENOX OR FOLIC ACID-B₆-B₁₂ PREVENTS SUBSEQUENT TRANSIENT MONOCULAR PARTIAL BLINDNESS. C.J. Glueck, K. Golnik, P. Wang, Cholesterol Center, Jewish Hospital, Department of Ophthalmology, University of Cincinnati Medical Center, Cincinnati, OH. In 8 men and 9 women (age 60 ± 14, all white) without ipsilateral atherosclerotic carotid plaque and with no other known causes of amaurosis fugax (AF), whose AF was associated with thrombophilia-hypofibrinolysis, we hypothesized that case-specific thromboprophylaxis (Coumadin-Lovenox, folic acid [5 mg]-B₆ [100 mg]-B₁₂ [2,000 µg], aspirin, cessation of exogenous estrogens, glucophage [2.5 g]) would prevent subsequent episodes of transient monocular partial or total blindness. All 17 cases had ≥ 1 thrombophilic-hypofibrinolytic disorder thought to be etiologic for AF. Seven cases had MTHFR C677T homozygosity or C677T-A1298C compound heterozygosity, 5 4G4G PAI-1 homozygosity, 4 high factor VIII, 4 lupus anticoagulant, 4 the platelet glycoprotein PL A1/A2 mutation, 2 low free protein S, 2 high plasminogen activator inhibitor activity (PAI-Fx), 1 V Leiden heterozygosity, 1 prothrombin gene (PTG) heterozygosity, and 1 protein C deficiency. In 4 cases on Coumadin for 16, 16, 21, and 98 months (1 PTG heterozygote, 1 protein C deficient [41%], 1 free protein S deficient [53%] with high factor VIII [157%], and 1 with high factor VIII [207%]), AF resolved, usually within 1 month of starting Coumadin, and the patients remained asymptomatic provided that the INR remained 2.5 or higher. In 1 case with low free protein S (28%), treated for 8 months of pregnancy and 1 month postpartum on Lovenox 80 mg/day, AF disappeared within 1 week, and she remained asymptomatic. In 3 cases with MTHFR C677T homozygosity treated with folic acid-B₆-B₁₂ for 10, 15, and 29 months, AF resolved, usually within 1 month of starting therapy, and has not recurred. AF stopped within 1 month in 2 cases (1 high factor VIII 157%, 1 PAI-1 4G4G, PL A1/A2) when exogenous estrogens-SERMES were discontinued and has not recurred. The frequency of AF events was reduced in 2 cases on aspirin alone (1 PL A1/A2, 1 high VIII 157%) and AF events have remained less frequent over 5 and 11 months on aspirin. In 1 case with hypofibrinolysis (4G4G PAI-1 polymorphism, high PAI Fx, 31.7 IU/mL) treated with Glucophage (2.55 g/day), symptoms resolved within 1 month and have not recurred in 9 months on Glucophage. When AF occurs in the absence of carotid artery atherosclerosis or other known causes of AF, thrombophilia and/or hypofibrinolysis are nearly universal, reversible pathoetiologies.

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STROMELYSIN-1 5A/6A AND eNOS T-786C POLYMORPHISMS, MTHFR C677T AND A1298C MUTATIONS, AND CIGARETTE-CANNABIS SMOKING: A PILOT STUDY OF GENE-ENVIRONMENT PATHOPHYSIOLOGICAL ASSOCIATIONS WITH BUERGER'S DISEASE. C.J. Glueck, M. Haque, M. Winiarska, S. Dharashivkar, R.N. Fontaine, B. Zhu, P. Wang, Cholesterol Center, Jewish Hospital, Cincinnati, OH. Buerger's disease (BD) etiologies are poorly understood. Beyond smoking cessation, medical-surgical treatments have limited success. We hypothesized that mutations associated with arterial vasospasm (stromelysin-1 5A/6A, eNOS T-786C) and C677T-A1298C methylenetetrahydrofolate reductase (MTHFR) interacted with cigarette-cannabis smoking, reducing vasodilatory nitric oxide (NO), promoting arterial spasm-thrombosis. Of 19 smoking BD patients (13 men [2 siblings], 6 women, 18 Caucasian, 1 African American), compared to 200 healthy Caucasian controls, BD patients were more likely to have 6A6A stromelysin-1 homozygosity (7/19 [37%] vs 46/200 [23%]) and to have eNOS T-786C homozygosity (3/19 [16%] vs 22/200 [11%]), but these patient-control differences were not significant, $p = .4$, 0.5. C677T MTHFR homozygosity or compound C677T-A1298C heterozygosity did not differ in patients vs controls (6/19 [32%] vs 70/200 [35%]), $p = .8$. In 9 patients who stopped and 1 who continued smoking, all stromelysin-1 5A/6A and/or eNOS heterozygotes-homozygotes, lower limb gangrenous ulcers, and intractable ischemic rest pain with arterial occlusion progressed despite conventional medical therapy, threatening amputation. In these 10 patients, to increase vasodilatory NO via endothelial NO synthase, L-arginine (15 g/day) was given, along with folic acid 5 mg, vitamin B₆ (100 mg), and B₁₂ (2,000 µg/day) to optimize homocysteine metabolism and reduce asymmetric dimethylarginine, a NO synthase inhibitor. Unexpectedly quickly and strikingly, within 8 weeks to 8 months on L-arginine-folic acid, all 10 treated patients improved with uniform pain reduction, ulcer healing, and in 5, full recovery of previously absent peripheral pulses. In smokers homo-heterozygous for stromelysin-1 5A/6A, eNOS T-786C, and C677T-A1298C MTHFR mutations, we speculate that the development and severity of BD are related to a gene-environment vasospastic interaction with reduced NO-mediated vasodilatation. Increasing NO production by L-arginine while optimizing homocysteine metabolism by folic acid-B₆-B₁₂ may have therapeutic benefit. Further blinded, placebo-controlled studies are needed to determine whether our observations can be generalized to larger BD cohorts.

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PLASMINOGEN ACTIVATOR INHIBITOR ACTIVITY, 4G5G POLYMORPHISM OF THE PLASMINOGEN ACTIVATOR INHIBITOR 1 (PAI-1) GENE, AND FIRST-TRIMESTER MISCARRIAGE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. C.J. Glueck, L. Sieve, B. Zhu, P. Wang, Cholesterol Center, Jewish Hospital, MDL Laboratories, Cincinnati, OH. We assessed whether hypofibrinolytic plasminogen activator inhibitor (PAI-Fx) was independently associated with first-trimester miscarriage in 430 women with polycystic ovary

syndrome (PCOS) who had previous pregnancies. We hypothesized that Glucophage optimizes live births in women with PCOS by lowering PAI-Fx before conception and further lowering PAI-Fx in the first trimester of pregnancy. We also assessed whether PAI-Fx levels were independently related to PAI-1 genotype and to modifiable risk factors, BMI, insulin, and triglyceride (TG). By stepwise logistic regression with the dependent variable being previous pregnancy outcomes at 3 levels (live birth pregnancies only [$n = 208$], both one or more 1 live births and ≥ one or more first-trimester miscarriages [$n = 111$] or first-trimester miscarriages only [$n = 71$]), and explanatory variables PAI-1 genotype, PAI-Fx, insulin, HOMA IR, BMI, and TG, PAI-Fx was positively associated with first-trimester miscarriage, $p = .004$. For each 5 IU/mL increment in PAI-Fx, the risk being in an adverse first-trimester miscarriage category increased, odds ratio 1.12, 95% CI 1.04 to 1.20. Prospectively, from pre-treatment to the last pre-conception visit on Glucophage, in 30 women who subsequently had live births, PAI-Fx fell 44% but rose 19% in 23 women with first-trimester miscarriage, $p = .03$. In the 30 women with live birth pregnancies, median PAI-Fx fell continuously from pretreatment through the first trimester (from 16.8 to 6.7 IU/mL), while PAI-Fx was either unchanged or rose in women with first-trimester miscarriage. Of the 921 PCOS women who had 4G5G data, 718 (78%) had 4G4G-4G5G genotypes vs 87/126 (69%) normal female controls ($\chi^2 = 4.95$, $p = .026$). The 4G-allele frequency was 53% in PCOS women vs 46% in controls ($\chi^2 = 4.3$, $p = .04$). By stepwise regression, positive independent determinants of PAI-Fx included BMI (partial $R^2 = 10.6\%$, $p < .0001$), insulin (partial $R^2 = 2.8\%$, $p < .0001$), TG (partial $R^2 = 1.1\%$, $p = .0009$), and PAI-genotype (partial $R^2 = 1\%$, $p = .0011$). The PAI-1 gene 4G polymorphism is more common in PCOS than normal women, and, in concert with obesity, hyperinsulinemia and hypertriglyceridemia, contributes to treatable, hypofibrinolytic, miscarriage-promoting, high PAI-Fx. Preconception and first-trimester decrements in PAI-Fx on Glucophage are associated with live births, whereas increments or no change in PAI-Fx despite Glucophage appear to be associated with first-trimester miscarriage.

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GROWTH, MOTOR, AND SOCIAL DEVELOPMENT IN BREAST- AND FORMULA-FED INFANTS OF METFORMIN-TREATED WOMEN WITH POLYCYSTIC OVARY SYNDROME. C.J. Glueck, M. Salehi, L. Sieve, P. Wang, Cholesterol Center, Jewish Hospital, Cincinnati, OH. **Objectives:** In a prospective, 6-month study of 61 breast- and 50 formula-fed infants born to 92 PCOS mothers, all of whom took metformin throughout pregnancy, our hypothesis was that metformin during lactation vs formula would have no adverse effects on infants' growth, motor-social development, and intercurrent illness. **Study Design:** Growth, motor-social development, and illness requiring a pediatrician visit were prospectively assessed in 61 nursing infants (21 male, 40 female) and 50 formula-fed infants (19 male, 31 female) born to 92 PCOS mothers taking a median of 2.55 g metformin/day throughout pregnancy and lactation. **Results:** Within gender, at 3 and 6 months of age, weight, height, and motor-social development did not differ ($p \geq .06$) between breast- and formula-fed infants. No infants had retardation of growth, motor, or social development. Intercurrent illnesses did not differ in 30% of breast- and 22% of formula-fed infants by 3 months ($p = .4$) and in 46% and 34% by 6 months ($p = .2$). **Conclusions:** Growth, motor-social development, and intercurrent illnesses in breast- and formula-fed infants from metformin-treated PCOS mothers did not differ; metformin during lactation appears to be safe and effective in the first 6 months of infancy.

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CHANGES IN WEIGHT, PAPILLEDEMA, HEADACHE, VISUAL FIELD, AND LIFE STATUS IN RESPONSE TO DIET AND METFORMIN IN WOMEN WITH IDIOPATHIC INTRACRANIAL HYPERTENSION. C.J. Glueck, K.C. Golnik, D. Aregawi, N. Goldenberg, L. Sieve, P. Wang, Cholesterol Center, Jewish Hospital, University of Cincinnati, College of Medicine, Ophthalmology Department, Cincinnati, OH. We hypothesized that metformin (MET)-diet would improve signs-symptoms of idiopathic intracranial hypertension (IIH) in women who also had polycystic ovary syndrome (PCOS) or hyperinsulinemia without PCOS. We prospectively assessed changes in weight, papilledema, headache, visual fields, and life status on 2.25 g MET-diet or diet alone for > 4 months in 75 women with IIH, 43 also having PCOS. Life status was graded by a self-reported 1-5 scale (1-well; 2-unwell, usual activities; 3-poor, usual activities; 4-poor, no usual activities; 5-totally disabled). Conventional Rx for IIH was maintained unchanged during MET-diet Rx. The diet was hypocaloric (1,500 kcal/day if BMI ≥ 25, 2000 cal/day if BMI < 25), high protein (26% of calories), low-carbohydrate (44%). Of the 43 PCOS cases, 31 received MET-diet, 12 diet only (not tolerate MET). Of the 32 cases without PCOS, 15 were hyperinsulinemic and received MET-diet, and 17 received diet alone. ($*p < .05$, $**p < .01$ vs baseline, within group).

| Group (n) | Hyperinsulinemic | | | |
|------------------------------------|------------------|----------------|------------------|-----------------|
| | PCOS +MET/2 (12) | PCOS+MET+ (31) | PCOS2/MET/2 (17) | PCOS2/MET+ (15) |
| Baseline BMI | 41.6 | 39.7 | 35.1 | 33.0 |
| Follow-up (months) | 11.1 | 14.0 | 21.2 | 16.3 |
| % Weight change | -2.5% | -6.5%** | -2.9% | -2.9%* |
| Papilledema at baseline | 10 (83%) | 28 (93%) | 13 (81%) | 13 (87%) |
| Papilledema at follow-up | 3 (25%)** | 7 (23%)** | 7 (44%)* | 4 (29%)** |
| Headache at baseline | 10 (91%) | 25 (83%) | 14 (87%) | 14 (93%) |
| Headache at follow-up | 6 (50%) | 20 (65%) | 10 (62%) | 10 (67%) |
| Visual fields (%better/same/worse) | 38/50/13% | 75/17/8% | 57/43/0% | 46/46/ 8% |
| Life status baseline → follow-up | 2.8 → 1.0 | 3.0 → 1.5** | 2.5 → 2.0 | 1.5 → 2.0 |

The greatest % weight loss occurred in diet-MET groups. MET ($p = .012$) and baseline BMI ($p = .019$) were predictors for weight loss. Papilledema improved in all 4 groups. The most marked improvement in life status ($p = .004$) was seen in the 31 women with PCOS on diet-MET. Since ~50% of women with IIH have PCOS, and since weight loss is central to IIH treatment, diet-MET is a novel approach to treat IIH in women with concurrent PCOS or hyperinsulinemia without PCOS.