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GASTROESOPHAGEAL REFLUX DISORDER: HIGH ADRENERGIC NEUROVASCULAR TONE WITH HIGH VAGAL TONE. O. Abdelmelek, R. Barndt, N. Mina, J. Iskarous, J. Huang, Bethel Public Service Clinic, Downey, CA.

Severe gastroesophageal reflux disorder (GERD) is poorly understood, precluding prevention therapy (Rx). Our pilot study (PS) shows that increases in adrenergic neurovascular (ANVT) and vagal tone (VT) cause severe GERD and reduction in ANVT decreases symptom levels (SL). Prospective studies (ProS) were done with a random sample of the general population with severe GERD as in PS. Severe GERD (reflux to pharynx) correlated with the following PS criteria: rise in pulse pressure (RPP) > 15 mm Hg (during handgrip at 5 psi/3min), systolic time intervals (STI) < 31% (24–30%), and resting heart rate (HR) at 60 ± 5 (predicts high VT). Serial measurements were made at time 1 and 2 (T1/2 = before/during 1 year Rx). Serial measurements were made of STI, HR10AM (HRA, peak ANVT), HR 12 noon (HRN, peak VT), % change in HR 10 am–12 noon (%CHR), systolic blood pressure (SBP), cardiac output (CO), systemic vascular resistance (SVR), and symptom levels (SL 1–100). Patients were 3/1 females/males, 18–70 years of age, all Caucasian. Exclusions were other gastric problems, fibromyalgia, diabetes, hypertension, and on other drugs. Controls (C) were normal, sex/age/race matched. Rx: diltiazem CD 240–360 mg/day, methyldopa 125–500 mg/day, and amitriptyline 10–100 mg/day, with double-blind crossover design. All data were placed into a blind matrix for analysis later. Severe GERD was predicted by STI of 24–30% by PS findings. **Results:** G means shown:

G	*#*	*RPP 1*	*STI 1/2*	*HRA 1/2*	*HRN 1/2*	*%CHR 1/2*	*SBP 1/2*	*CO 1/2*	*SVR 1/2*	*SL 1/2*
PS	50	20*	26*/42	95*/72	60/65	37**/10	103/105	2.6/4.4	2154*/1091	91*/10
ProS	100	22*	27*/44	98*/73	64/66	36**/9	105/110	2.8/4.6	2057*/1339	94*/8
C	100	9	53/54	72/74	67/70	7/6	110/108	5.3/5.1	1162/1176	0/0

*Significant (Sig) difference from C at $p < 0.01$, **Sig change from 10–12 am at $p < .02$, both by *t*-test. STI = PEP/LVET × 100%.

ProS results confirm PS results showing that severe GERD was found in people with high ANVT, during a shift to high vagal tone, with Sig reduction in HR from peak ANVT at 10 am to peak VT at 12 noon. Basilar artery migraine was also found in 95% of ProS patients with high ANVT and high vagal tone. SL of ProsS patients were significantly reduced by Rx. Thus, GERD is due to high ANVT with increased vagal tone and can be prevented with therapy.

2

WEIGHT LOSS IS A FEATURE OF PROTRACTED METFORMIN THERAPY IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. M. Agloria, M. Winiarska, G. Luo, M. Salehi, L. Sieve, D. Aregawi, P. Wang, C.J. Glueck, Cholesterol Center, Jewish Hospital, Cincinnati, OH.

In 296 women with polycystic ovary syndrome (PCOS) treated with metformin (MET 2.3 ± 0.4 g/day [Rx]) and diet (1,500 calories/day if BMI < 25, 2,000 calories if BMI ≥ 25 [protein 26% of calories, carb 44%]) for 1, 2, and 3 years, we assessed whether and to what degree weight loss was a feature of 1, 2, and 3 years of MET-diet Rx in women with PCOS.

		Group Weight Change					Group			
Duration Rx	n	*Age*	*BMI*	*Wt Pre-Rx*	*Wt on Rx*	*%Wt Change*	*5–10%*	*10–15%*	*15–20%*	*> 20%*
1 yr	229	30	35.8	95 kg	90 kg	5.9%	28%	16%	9%	2%
2 yr	127	31	34.6	93 kg	88 kg	5.8%	26%	15%	8%	6%
3 yr	94	31	35.0	93 kg	87 kg	6.3%	30%	12%	9%	7%

Despite pretreatment (Pre-Rx) group severe obesity, MET-diet was successful in producing group weight reductions of 5.9% at 1 year, 5.8% at 2 years, and 6.3% at 3 years. Weight loss ≥ 5% was realized by 55% of women at 1 year, 55% at 2 years, and 58% at 3 years, with 15% or more weight loss in 11% of women at 1 year, 14% at 2 years, and 16% at 3 years. At years 1–3 on Rx, weight fell ($p < .05$) in BMI groups 25–30 (overweight), 30–40 (obese), and ≥ 40 (severely obese), and at year 1, in BMI group < 25 (normal). At 1 year follow-up on MET-diet, by stepwise regression, with change in weight as the dependent variable and Pre-Rx weight, age, duration of Rx, and MET dose as the explanatory variables, Pre-Rx weight was a significant positive explanatory variable ($p = .017$). At 1, 2, and 3 years follow-up on MET-diet, median group HOMA insulin resistance (IR) fell 28% ($p < .0001$), 42% ($p < .0001$), and 52% ($p < .0001$), triglycerides (TG) fell 16% ($p = .010$), 12% ($p = .017$), and 19% ($p = .011$), LDL cholesterol (LDLC) fell 5% ($p < .0001$), 4% ($p = .033$), and 8% ($p = .014$), systolic blood pressure (SBP) fell 4% ($p = .0004$), 3% ($p = .037$), and 3% ($p = .20$), diastolic blood pressure (DBP) fell 6% ($p < .0001$), 0% ($p = .30$), and 3% ($p = .08$). By stepwise regression with explanatory variables age, duration of Rx, MET dose, and weight loss, weight loss was a significant positive explanatory variable for reduction in HOMA IR (year 1 $p = .023$, year 2 $p = .012$), was associated with reduction in TG (year 1 $p = .005$, year 2 $p = .007$, year 3 $p = .043$), was associated with reduction in SBP (year 1 $p = .0001$, year 2 $p = .046$), and was associated with reduction in DBP (year 1 $p = .0001$, year 2 $p = .016$). MET-diet for 1, 2, and 3 years in women with PCOS effectively and safely reduces weight and major atherogenic components of the metabolic syndrome.

3

HISPANICS WITH THE METABOLIC SYNDROME SHOWED HIGHER INCIDENCE OF ATRIAL FIBRILLATION. P.I. Altieri, H.L. Banchs, M. Crespo, N. Escobales, Y. Figueroa, J.C. López, J. Hernández, H. Mundo, P. Casillas, University of Puerto Rico, San Juan, Puerto Rico.

Atrial fibrillation (AF) is the most frequent arrhythmia after the sixth decade. The incidence in (P) with metabolic syndrome (MS) and diabetes mellitus type II (DM) is not known. A retrospective analysis was undertaken in 173 p. with MS-DM with insignificant coronary disease. The mean age was 60 years. 57% were males and 42.5 females. The mean blood sugar on admission was 169 mg/dL. The mean body mass was 30 kg/m². The ejection fraction was subnormal (52 ± 8%) when compared to our normal group (62 ± 12%), $p < .0001$. The end-systolic dimension of the left atrium was higher in the MS-DM (46 ± 10 mm) when compared to the normal group (40 ± 8 mm), $p < .05$. The incidence of (AF) in the MS was 12.9% when compared to the control group (5.9%), $p < .001$. Causes of this higher incidence are (1) ischemia to the sinus node due to atherosclerosis or vasoconstriction of the sinus node (SN) artery due to an elevated concentration of angiotensin II peripherally, intracoronary, and in the atrial tissue; (2) remodeling of the SN due to left ventricular dysfunction; (3) remodeling of the left and right atrium; (4) hyperinsulinemia influencing the SN through NA^+-K^+ ATPase; (5) aging; (6) abnormalities of QT dispersion. All of these mechanisms will be discussed.

4

SUCCESS OF METFORMIN-PIOGLITAZONE IN RESOLVING ENDOCRINOPATHY AND INSULIN RESISTANCE-HYPERINSULINEMIA IN 40 WOMEN WITH POLYCYSTIC OVARY SYNDROME NOT OPTIMALLY RESPONSIVE TO METFORMIN ALONE. D. Aregawi, M. Salehi, M. Agloria, M. Winiarska, L. Sieve, P. Wang, C.J. Glueck, Cholesterol Center, Jewish Hospital, Cincinnati, OH

In 40 women (36 white, 1 black, 3 other) with polycystic ovary syndrome (PCOS) not optimally responsive to metformin (MET 2.55 g/day) for 1 year, endocrine and menstrual response to MET (2.55 g) with added pioglitazone (PIO 45 mg/day) for 1 year were compared to outcomes on MET alone. Before MET, 35% of women were obese with BMI 30.0 to < 40 and 48% had BMI 40 or higher (severely obese). In the year before MET, the mean ± SD (median) of expected menses was only 23 ± 27% (median 17%), rising to 44 ± 41% (median 33%) after 1 year on MET ($p = .002$), then rising to 81 ± 30% (median 100%) after 6 months on MET-PIO ($p < .0001$), 76 ± 33% (median 100%) at 9 months, and 78 ± 35% (median 100%) at 12 months. Before MET, mean ± SD weight was 106 ± 28 kg and median BMI 37.6 kg/m². After 1 year on MET weight fell (104 ± 28 kg, $p = .01$) but increased on MET-PIO (106 ± 29 kg, $p = .03$). On MET for 1 year, median DHEAS fell nonsignificantly ($p = .75$) from median 224 to 201 µg/dL but then fell to 169 µg/dL on MET-PIO ($p = .03$). Median sex hormone binding globulin (SHBG) was 25 nmol/L before MET, 20 on MET ($p > .1$), and rose to 27 on MET-PIO ($p < .001$). Median fasting serum insulin was 20.2 µU/mL before MET, 20.1 on MET ($p > 0.1$), but then fell to 13.1 µU/mL on MET-PIO ($p < .001$). HOMA insulin resistance was 3.90 before MET, 4.76 on MET ($p > .1$), but then fell to 2.74 on MET-PIO ($p < .001$). HOMA insulin secretion was 285 before MET, 217 on MET ($p > .1$), but then fell to 159 on MET-PIO ($p < .001$). HDL cholesterol, 41 mg/dL before MET, 40 mg/dL on MET ($p > .1$), rose to 44 mg/dL on MET-PIO ($p < .001$). In obese and severely obese women with PCOS who do not optimally respond to MET, addition of PIO to MET (despite weight gain) promotes much more regular menses, lowers DHEAS, elevates SHBG, lowers fasting serum insulin, lowers HOMA insulin resistance and HOMA insulin secretion, and elevates HDL cholesterol. Combination of the insulin-sensitizing agents MET and PIO successfully resolves endocrinopathy and insulin resistance-hyperinsulinemia in obese women with PCOS who are not optimally responsive to MET alone.

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SIGLEC-7 IS HIGHLY AND SIMILARLY EXPRESSED ON TH1 AND TH2 LYMPHOCYTES. P. Beerelli,[1] S.B. Meyers,[2] L.M. Mitchell,[3] S.D. Ghimbovschi,[3] E.P. Hoffman,[1,3] R.J. Freishtat,[1,3,4] [1]School of Medicine and Health Sciences, George Washington University, Washington, DC; [2]University of California-Davis, Davis, California; [3]Research Center for Genetic Medicine, Children's National Medical Center, Washington, DC; [4]Division of Emergency Medicine, Children's National Medical Center, Washington, DC.

Purpose: Siglec-7 is an NK-receptor that negatively regulates cell activation via its intracellular tyrosine-based inhibitory motif (ITIM) when bound to its ligands, sialic acid-containing glycans of glycoproteins and glycolipids. Recent reports identified Siglec-7 on T cells and showed that it is capable of negative regulation of TCR signaling. As part of a larger study identifying novel differentiating markers between TH1 and TH2 lymphocytes in respiratory illness, we aimed to determine whether Siglec-7 is differentially expressed between TH1 and TH2 lymphocytes. **Methods:** A novel antibody cocktail was used to negatively enrich TH1 and TH2 cells from the PBMCs of healthy volunteers. Microarrays allowed determination of differential gene expression. RT-PCR was performed for selected targets. Protein markers were studied using flow cytometry before and after activation. **Results:** Isolates were > 95% pure TH cells with enriched TH1 (90.3%) and TH2 (84.1%) subsets. Expression profiling showed differential expression of Siglec-7 mRNA between TH1 and TH2 cells (TH1:TH2 ratio = 3.1). RT-PCR showed lower expression of Siglec-7 in TH1 cells (TH1:TH2 = 0.64 ± 0.06). Flow studies of resting and activated TH1 and TH2 lymphocytes showed increased expression of Siglec-7 from (mean ± SEM) 59.7 ± 16.5% of cells (mean fluorescence intensity = 24.1 ± 3) to 43.4 ± 24% of cells (19.3 ± 4.5) (p = NS) for TH1 cells and from 70.4 ± 13.3% of cells (48.3 ± 5.6) to 48.2 ± 24.5% of cells (29.6 ± 3.2) (p = NS) for TH2 cells. **Conclusions:** We found marked expression levels of Siglec-7 on both quiescent and activated TH1 and TH2 fractions. The abundance of this receptor suggests that it may play an important role in regulating TH cell activation as it does on NK cells. This also implies that there may be value in examining the role of TH cell Siglec-7 in the immune response to influenza A and B, which express neuraminidase, a sialidase that cleaves sialic acid from glycoproteins.

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RELATIONSHIP BETWEEN SERUM CARNITINE AND PLASMINOGEN ACTIVATOR INHIBITOR 1 IN AFRICAN AMERICAN HEMODIALYSIS PATIENTS. R.E. Brown, D. Haria, M. Zimpa, P. Murty, J. Lazar, L. Salciccioli, M.O. Salifu, SUNY Downstate Medical Center, Brooklyn, NY.

Elevated plasminogen activator inhibitor 1 (PAI-1) has been associated with cardiovascular disease in hemodialysis patients. Carnitine, an amino acid–derived nutrient, is often decreased in hemodialysis patients and is associated with dilated cardiomyopathy and peripheral vascular dysfunction. The aim of this study was to determine a relationship between serum carnitine and PAI-1 levels and the composite cardiovascular end point (a

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