

Monday, October 11, 2010

Viewing: 11:30 am – 6:30 pm

Presenters at Posters: 12:30 pm – 1:30 pm

Location: Room 28

**Nutraceuticals and Obesity****724-P****Green Tea Extract: Ameliorating Metabolic Abnormalities Induced By High-Fat Diet in C57 Mice**Jingzhong Wang, Yingjie Yu *Beijing, China*; Shinichi Meguro, Satoshi Hayashi, Mitsuhiro Katashima, Takeshi Yasumasu *Tokyo, Japan*; Keji Li *Beijing, China*

Objective: To investigate the effects of long-term intake of green tea extract (GTE) containing relatively low doses of tea catechins on the metabolic abnormalities induced by high-fat diet in C57 mice. Method: C57BL/6J were divided into five groups at random and given a diet of low-fat, high-fat, high-fat supplemented with GTE containing 0.1%, 0.2%, 0.3% (w/w) tea catechins, respectively, for 155 days. We compared the food intake, body weight, visceral fat weight and serum lipids, glucose, leptin, insulin, free fatty acid in non-fasting condition between groups. Results: Metabolic abnormalities were seen in C57 of a high-fat diet with significant increase in body weight, visceral fat tissues, serum leptin and serum glucose ( $P < 0.05$ ). Supplementation of GTE could significantly reduce the final body weight and body weight gain ( $P < 0.05$ ) without significant influence on food intake. The low and high dose caused a significant reduction in epididymal, perirenal and retroperitoneal fat weight or its proportion to body weight ( $P < 0.05$ ). GTE had no significant effects on serum lipids, insulin or free fatty acid, but caused a significant reduction of leptin ( $P < 0.05$ , in all dose groups) and glucose ( $P < 0.05$ , only in the low dose group). Conclusion: Supplementation of GTE containing 0.1%-0.3% tea catechins for 5 months has ameliorative effects on metabolic abnormalities induced by high-fat diet with the reduction of body weight gain, visceral fat accumulation, serum leptin and glucose level.

**725-P****Curcumin Reduced Visceral Fat After Ovariectomy**Hye-Seon Choi, Ke Ke, Woon-Ki Kim *Ulsan, Korea*

There is growing evidence of a connection between fat and bone metabolism at both the clinical and molecular levels, although the systemic regulators of fat and bone metabolism have not been clearly identified. The relationship between obesity and bone loss, two metabolic derangements of fat and bone metabolism, is controversial, and the relationship between body weight and bone mineral density (BMD) is complex. Osteoporotic postmenopausal women have higher levels of lipid (Broulik and Kapitola, 1993), and a lipid-lowering drug, Statin, increases BMD in clinical studies (Uzzan et al., 2007), suggesting a negative relationship between BMD and fat. Curcumin (diferuloylmethane), a pigment derived from turmeric, acts as an antioxidant. Oral injection of curcumin increased bone density and reduced visceral fat after ovariectomy. Curcumin also decreased bone marrow adiposity, suggesting that curcumin inhibits adipogenesis by increasing osteoblast differentiation. Reduced fat could be at least partly due to the favored differentiation shift to osteoblast differentiation. This work was supported by a KHIDI Grant (A090080), a KOSEF grant (R012007000210820), and NRKRF Grants (2009-0066232; 2009-0087350) funded by the Korean government.

**726-P****Piperine Ameliorates Obesity and Regulates Molecules Involved in Energy Expenditure and Endoplasmic Reticulum Stress in Mice Fed a High-fat Diet**Yoojeong Jin, Soyoung Park, Taesun Park *Seoul, South Korea*

Piperine is a nitrogenous pungent substance presents abundantly in the fruits of piper species. The main objective of this study was to elucidate the anti-obesity effects of piperine. We also hypothesized that consumption of piperine could modulate the expression of genes underlying energy expenditure, endoplasmic reticulum (ER) stress and inflammation in visceral adipose tissue of mice. In male C57BL/6N mice fed a high-fat diet (HFD) to induce obesity, supplementation with piperine (0.5 g/kg

diet) for 10 weeks reduced body weight gain, visceral fat-pad weight, and plasma levels of cholesterol, triglyceride and free fatty acid. The expression levels of thermogenic uncoupling protein 1 as well as their regulators, such as peroxisome proliferator-activated receptor (PPAR)  $\alpha$ ,  $\beta$ , and PPAR  $\gamma$  coactivator 1 $\alpha$ , in the visceral adipose tissue of mice, which were down-regulated by HFD, were normalized by feeding piperine. Dietary piperine supplementation increased the phosphorylation of AMP-activated protein kinase and acetyl-CoA carboxylase proteins and the mRNA level of carnitine palmitoyltransferase 1, key enzymes of fatty acid oxidation. The protein level of phospho-eukaryotic translation initiation factor 2 $\alpha$ , a marker of ER stress, was decreased in piperine supplemented mice. Furthermore, down-regulations of spliced X-box binding protein 1, activating transcription factor 6, tumor necrosis factor  $\alpha$  and interleukin-6 were documented with RT-PCR. These results suggest that piperine effectively ameliorates obesity mediated via the regulation of multiple genes involved in energy expenditure and ER stress.

**727-P****Carvacrol Inhibits Hepatic Steatosis By Suppressing Lipogenesis and Inflammation in Mice Fed a High-Fat Diet**Yunjung Kim, Soomin Cho, Soyoung Park, Eunhyung Kim, Taesun Park *Seoul, South Korea*

Carvacrol, a monoterpene phenolic constituent of essential oil produced by numerous aromatic plants and spices, is known to possess a range of bioactive and medicinal activities, such as anti-microbial, anti-tumor, anti-thrombotic, anti-inflammatory and hepatoprotective properties. We investigated whether carvacrol supplementation could reduce hepatic steatosis in mice fed a high-fat diet (HFD) and this hepatoprotective effect of carvacrol might be dependent on its anti-lipogenic and anti-inflammatory activities. Mice were fed either a normal diet, HFD (40% energy as fat) or carvacrol supplemented diet (1 g/kg diet) for 10 weeks. The HFD mice developed hepatomegaly and hepatic steatosis with elevated plasma alanine aminotransferase and aspartate aminotransferase activities. Carvacrol supplementation led to complete normalization of those biomarkers for non-alcoholic fatty liver disease. Furthermore, the decrease in hepatic fat accumulation by carvacrol was likely due to an inhibition of lipogenesis, as evidenced by down-regulated hepatic mRNA levels of key lipogenic transcription factors, such as peroxisome proliferator-activated receptor  $\gamma$ 2, sterol regulatory element-binding factor 1c, CCAAT/enhancer binding protein  $\alpha$  and liver X receptor, and their target genes including adipocyte protein 2, lipoprotein lipase and fatty acid translocase. In addition, increased mRNA levels of proinflammatory cytokines (tumor necrosis factor  $\alpha$ , interferon  $\beta$  and interleukin 1 $\beta$ ) observed in the livers of HFD-fed animals were significantly decreased by carvacrol. These results suggest that carvacrol effectively ameliorated hepatic steatosis induced by a HFD mediated via the regulation of multiple hepatic genes involved in lipogenesis and inflammation.

**728-P****Dietary Canola/Flax Oil Blend Attenuates Components of the Metabolic Syndrome in Diet-Induced Obese (DIO) Rats**Danielle P. Durston, Peter C. Zahradka, Carla G. Taylor *Winnipeg, Canada*

The metabolic syndrome is characterized by obesity, insulin resistance, hypertension, dyslipidemia, and more recently, inflammation and hepatic steatosis. Given the current obesity epidemic and the widespread consumption of fats in the diet, there is an urgent need to identify dietary fats that can attenuate metabolic syndrome parameters. More information is needed on how monounsaturated fatty acids (MUFAs) present in canola oil and plant-based omega-3 polyunsaturated fatty acids (e.g. alpha-linolenic acid =ALA) present in flax oil may modulate components of the metabolic syndrome. The objective of the present study was to investigate the effects on metabolic syndrome parameters in 6 week old Obese Prone Sprague Dawley rats fed high fat (55% energy) diets containing various fat types including high oleic canola oil (HOC), canola oil (C), a canola/flax oil blend (C/F), safflower oil (SF), soybean oil (SB), or lard (L) for 12 weeks. The HOC, C, and C/F groups had the lowest total weight gain. Similarly, the HOC, C, C/F, and SF groups had the lowest fasting serum glucose, and the C/F and the SF groups had the lowest fasting serum triglyceride. Additionally, the C/F group had the lowest percent hepatic fat and the lowest fasting serum haptoglobin, a marker for inflammation. Conversely, no difference was seen between groups in terms of blood pressure, or oral glucose

tolerance. In conclusion, the canola/flax oil diet, which contained high amounts of MUFA and ALA, attenuated weight gain, glycemia, lipidemia, inflammation and hepatic steatosis in DIO rats, a model for the metabolic syndrome.

**729-P****Comparison of the Glycemic Response of Two Animal Models to Botanical Inhibitors of Carbohydrate Digestion**

Lisa Reaves, Mary-Beth Skelding *Columbus, OH*

Zucker obese (ZO) and Zucker Diabetic Fatty (ZDF) rats are pre-clinical models of insulin resistance and diabetes, respectively. This study examined each model's response to carbohydrate digestion inhibitors by using meal tolerance tests (MTT). ZO and ZDF were each treated with botanical extracts with  $\alpha$ -glucosidase inhibitor activity. The extracts, *Salacia oblonga* root (SO) or *Morus* spp. leaf (MS), were delivered in a carbohydrate meal. Ten week old male ZO and ZDF rats were used in four experiments. For each experiment, the animals were assigned to two groups of 10 matched by fed body weight. Overnight-fasted rats were gavaged with a Control or Experimental meal. Control was maltodextrin (2 g/kg-body weight (BW)). Experimental was maltodextrin at the same dose plus either SO (75 mg/kg-BW) or MS (50 mg/kg-BW). Tail blood [glucose] was measured before treatment (fasted) and every 30 minutes for 2 hours thereafter. Glucose area-under-the curve ( $AUC_{120}$ ) values were calculated. Means were compared with Student's t-test. SO decreased  $AUC_{120}$  by 36.3% compared to control in ZO ( $p < 0.005$ ) and by 49.7% compared to control in ZDF ( $p < 0.005$ ). MS decreased  $AUC_{120}$  34.5% compared to control in ZO ( $p < 0.005$ ). However, MS decreased  $AUC_{120}$  only 4.2% compared to control in ZDF (NS). Because ZO and ZDF rats reacted similarly to SO treatment, it was expected that both models would respond correspondingly to MS treatment, however, this was not the case. The physiological response to carbohydrate digestion inhibitors may vary among similar animal models.

**Integrated Biology of Obesity – Translational Studies****730-P****Are Shorter Rodent Longevity Studies Feasible, and What Is the Required Increase in Sample Size?**

Henry T. Robertson, Daniel Smith, Nicholas Pajewski, David B. Allison *Birmingham, AL*

Many longevity experiments have been performed using rodents to assess the effects of diets, drugs, genes, toxins, and other factors on lifespan. A great challenge with such experiments is their long duration – typically over 3.5 years given rodent lifespans. This imposes significant costs in terms of time until answers can be obtained. We collected longevity data from 15 rodent studies and artificially truncated them at 2 years to assess the extent to which one will obtain the same answer regarding effects on overall mortality. When truncated, the point estimates were not significantly different in any of the treatment groups. This implies that in most cases, 2-year and full lifespan studies can be expected to yield the same estimates. On average, the variances of coefficients from truncated studies were approximately 5 times larger than full-length studies, implying that a truncated study with 5 times more rodents will have equivalent power.

**731-P****Association Between Insulin Resistance and Macrophage-Mediated Inflammation in Subcutaneous and Visceral Fat Depots in Obese Individuals**

Sherman J. Bigornia, Melissa G. Farb, Melanie M. Mott, Lija Joseph, Donald T. Hess, Caroline M. Apovian, Joseph Vita, Noyan Gokce *Boston, MA*

Macrophage-mediated adipose tissue inflammation has been linked to the pathophysiology of insulin resistance. While experimental studies suggest that inflammation within visceral depots relate more to metabolic dysfunction than subcutaneous fat, there is limited information in human disease. We examined the relationship between systemic insulin resistance and degree of depot-specific adipose tissue inflammation in subcutaneous, omental, and mesenteric fat in obese subjects undergoing gastric bypass. Using immunohistochemistry, we categorized individuals as having inflamed or non-inflamed fat by the presence (+) or absence (-) of macrophage crown-like structures (CLS), respectively. Subjects were

analyzed by tertiles of HOMA in relation to CLS+ status by fat depot. We also categorized individuals as 1) CLS- in all depots, 2) CLS+ in 1-2 depots, or 3) CLS+ in all depots, and related to insulin sensitivity. Fat tissue from all three depots was collected from 47 individuals (87% female, age  $42 \pm 11$  yr, BMI  $47 \pm 8$  kg/m<sup>2</sup>). The prevalence of CLS+ status increased by HOMA tertile in all depots as follows: subcutaneous (40%, 81%, and 94%;  $p < 0.05$ ), omental (40%, 56%, and 81%;  $p = 0.06$ ), and mesentery (40%, 81%, and 94%;  $p < 0.05$ ). Subjects CLS+ in all depots exhibited higher HOMA ( $n = 24$ ; HOMA =  $4.8 \pm 1.7$ ) as compared to subjects who were CLS+ in 1-2 depots ( $n = 17$ ;  $2.3 \pm 2.0$ ;  $p < 0.05$ ) and CLS- in all depots ( $n = 6$ ;  $2.2 \pm 1.9$ ;  $p < 0.05$ ). These findings show that the degree of adipose inflammation in all depots relates to systemic insulin resistance. The results also suggest that proinflammatory changes in subcutaneous fat occur in parallel with immune activation of visceral depots.

**732-P****Validation of the Effects of the PNPLA3 Gene on Liver Fat Deposition in Overweight and Obese Children and Teenagers**

Michael I. Goran, Ryan W. Walker, Kim-Anne Le, Swapna Mahurkar, Jaimie N. Davis *Los Angeles, CA*; Donna Spruijt-Metz *Alhambra, CA*; Marc J. Weigensberg, Hooman Allayee *Los Angeles, CA*

Objective: A recent genome-wide study in adults identified an amino acid substitution (C to G) in the adiponutrin (PNPLA3) gene, associated with ~2-fold higher liver fat. This effect was strongest in Hispanics in whom the frequency of the variant was much higher than African Americans (48% vs 10%). We sought to examine these associations in children. Research Design & Methods: 260 subjects aged 8–18y (188 Hispanics/72 African Americans) were genotyped and assessed for visceral (VAT) and subcutaneous adipose tissue (SAT) volume and hepatic (HFF) and pancreatic fat fraction (PFF) by MRI. An additional group of 227 Hispanic children were genotyped to examine the influence of PNPLA3 on insulin sensitivity and fasting lipids. Results: Genotype distributions were significantly different in Hispanics (28%GG/47%CG/24%CC) compared to African Americans (0%GG/15%CG/85%CC). In Hispanics, HFF in GG subjects was 78% and 136% higher than GC and CC respectively ( $11.1 \pm 0.8$  in GG vs  $6.6 \pm 0.7$  in GC and  $4.7 \pm 0.9$  in CC;  $p < 0.0001$ ), and this effect was observed even in the youngest children (8-10 years). The variant was not associated with VAT, SAT, PFF, or insulin sensitivity or glucose/insulin response to an oral glucose challenge. However, Hispanic children with GG had significantly lower HDL-cholesterol ( $40.3 \pm 10.2$  in CC vs  $36.2 \pm 7.4$  in CG vs  $35.0 \pm 7.1$  in GG;  $p = 0.001$ ). Conclusions: These results provide new evidence that the effect of this variant is manifested early in life, is unique to fat deposition in liver and is also associated with low HDL-cholesterol.

**733-P****Glucose, Insulin, Leptin, Ghrelin, Cortisol, Dehydroepiandrosterone-Sulfate and Satiety During Two Days of Near Complete Energy Restriction**

Stefan M. Pasiakos, Christina M. Caruso *Natick, MA*; Mark D. Kellogg *Boston, MA*; F. Matthew Kramer, Harris R. Lieberman *Natick, MA*

Few studies have systematically characterized the endocrine response and regulation of satiety in response to acute, severe energy restriction. Using a double-blind, placebo-controlled crossover design, we assessed the effects of 48 h near complete energy restriction on endocrine regulators of appetite, stress hormones, and their association with satiety. Twelve men and 1 woman participated in this controlled 2 d, diet intervention study in both a fully fed (FED) and calorie deprived condition (CAL-DEP; < 10% of estimated energy requirements). Test meals indistinguishable in sensory characteristics were provided. Glucose, insulin, leptin, ghrelin, cortisol, dehydroepiandrosterone-sulfate (DHEA-S) and satiety were repeatedly assessed. Mean glucose, insulin, and leptin concentrations were lower ( $P < 0.0001$ ) for CAL-DEP compared to FED. Ghrelin and DHEA-S were higher ( $P < 0.0001$ ) for CAL-DEP relative to FED. Cortisol levels declined over each day regardless of diet ( $P < 0.0001$ ) but were 32% higher ( $P < 0.01$ ) at the conclusion of the study for CAL-DEP compared to FED. Satiety was 25% lower ( $P < 0.0001$ ) for CAL-DEP relative to FED and decreased ( $P < 0.0001$ ) over time regardless of diet. In the FED state, insulin ( $r = 0.55$ ), glucose ( $r = 0.76$ ), cortisol ( $r = -0.59$ ), and DHEA-S ( $r = -0.62$ ) were associated ( $P < 0.05$ ) with satiety, but not during

CAL-DEP. In conclusion, 2 days of severe energy restriction alters some endocrine regulators of appetite and stress hormones. Levels of perceived satiety were associated with several hormones during energy balance but not during caloric deprivation.

### 734-P

#### Impact of Dietary Intake on Liver Fat Depots Among Variants in PNPLA3 in Overweight Latino Youth

Jaimie N. Davis, Hooman Allayee, Kim-Anne Le, Ryan W. Walker, Susanna Vikman *Los Angeles, CA*; Donna Spruijt-Metz *Alhambra, CA*; Marc J. Weigensberg, Michael I. Goran *Los Angeles, CA*

**Objective:** Recently, a genetic variant (rs738409; C>G) of the PNPLA3 gene was associated with increased liver fat deposition, with a more pronounced effect in Latinos. Our aim was to examine whether the relationship between dietary intake and liver fat content was influenced by PNPLA3 genotype in overweight Latino children. **Methods:** Genotyping of PNPLA3 was performed in 145 children (74% female, 8-18 yrs) using Taqman methodology. Dietary intake was assessed by 3-day diet records. Visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and liver fat were assessed by MRI using multiple abdominal slices. General linear modeling was used to assess genotype by diet interactions on liver fat. The following a priori covariates were included in each model: gender, age, energy, VAT, and SAT. **Results:** Frequencies of the GG, CG and CC genotypes were 30%, 46% and 24%, respectively and liver fat was ~2-fold higher in GG. Liver fat was positively related to carbohydrate ( $r=0.38$ ;  $p=0.02$ ) and total sugar intake ( $r=0.33$ ;  $p=0.04$ ), and inversely related to protein ( $r=-0.35$ ;  $p=0.03$ ) and fat intake ( $r=-0.31$ ;  $p=0.05$ ) only in subjects with the GG allele, independent of VAT and SAT. No dietary variables were related to liver fat in the CC or CG groups. **Conclusions:** These findings suggest that Latino children carrying the GG allele are susceptible to increased liver fat when dietary carbohydrate intake is high and fat and protein intake are low. Specific dietary interventions based on genetic predisposition in this population may lead to more effective therapeutic outcomes for fatty liver.

### 735-P

#### Effects of Appetite on the Neuronal Response to Visual Food Stimuli in Japanese Young Men; An fMRI Study

Tohru Yamaguchi, Masanobu Hibi, Yayoi Yoshimoto, Mitsuhiro Katashima *Tokyo, Japan*; Li-qun Wang, Shinya Kuriki *Inzai-City, Japan*

**Background:** Appetite is a fundamental desire of human life. However the studies for Japanese subjects focusing on the relationship between appetite and the brain activity are rarely found in literature. This study was aimed to find the difference in the activation region in between a state of hunger and a full stomach in healthy young Japanese men, utilizing functional magnetic resonance imaging (fMRI). The difference in activations between high-caloric foods and dessert foods were also studied. **Methods:** The fMRI study was based on block-design in which two types of images from selected foods i.e., high-caloric foods and desserts, were presented to subjects. Mosaic images derived from these food images were used as control stimuli. Two fMRI imaging sessions were conducted; one after more than 16 hours fasting, and the other 30 minutes after ingestion of a milkshake. **Results:** Data of thirteen subjects (BMI,  $21.9 \pm 2.6$  kg/m<sup>2</sup>) were analyzed using SPM8. A comparison between the high-caloric image and control image indicated BOLD activation of thalamus and parts of the limbic system such as amygdala and cingulate cortex ( $p<0.001$ , uncorrected) during the state of hunger. The result from the paired t-test indicated higher activation of the limbic system in the hunger than full state. In contrast, the activations by dessert food stimuli were found in more extended regions when the subject was full. **Conclusion:** The results demonstrated the activation of thalamus/limbic system for visual stimulation of high-caloric foods in hunger state and distinct activation in full state for Japanese young subjects.

### 736-P

#### Comparison of Free Fatty Acid Response to Glucose and Insulin in Black African, African American and White Women

Carson C. Chow, Anne E. Sumner *Bethesda, MD*; Gloria L. Vega *Dallas, TX*; Gyorgy Csako, Madia Ricks, Bernard V. Miller, Vipul Periwal *Bethesda, MD*

Racial differences in plasma free fatty acid responses to glucose and insulin could give insights to possible health disparities between races. Here, we compare differences in free fatty acid (FFA) clearance rates between Black Africans living in the United States, African Americans and Whites. Fifty

five women (21 Black Africans, 17 African Americans, 17 Whites), age  $35 \pm 10$  y, mean  $\pm$  SD, BMI  $29.1 \pm 6.3$  kg/m<sup>2</sup>, had insulin modified-frequently sampled intravenous glucose tolerance tests with plasma glucose, insulin and FFA determined at 32 time points in 3h. A three-compartment model was fit to the time series of FFA and glucose with insulin as the input for the first 2h. The model was an extension of the classic minimal model for glucose disposal modified to include FFA appearance due to lipolysis and FFA clearance through first order kinetics. Lipolysis was inhibited by insulin acting through a remote compartment. The model predicted that African Americans had a higher FFA clearance rate than Whites ( $0.083 \pm 0.05$  min<sup>-1</sup> v  $0.13 \pm 0.06$  min<sup>-1</sup>,  $P<0.01$ ) and neither was significantly different from Black Africans ( $0.10 \pm 0.06$  min<sup>-1</sup>). There were no significant differences among the groups for the parameters governing lipolysis and suppression of lipolysis by insulin. The health implications of greater FFA clearance in African American women await investigation.

### 737-P

#### Inhibition of the Cannabinoid-1 Receptor Induces Weight Loss in an Experimental Canine Model By Reducing Food Intake Without Adaptive Lowering of 24-Hour Energy Expenditure

Steven Heymsfield, Susan Nicolich, Amy Johnson-Levonas, Tung Fong, Joana Achanfuo-Yeboah, Paul Cunningham, Donald Hora, Donald Thompson, Gerry Hickey, Terry Faidley, Alison Strack *Rahway, NJ*

**Background:** Cannabinoid-1 receptor (CB1R) inhibition promotes greater weight loss than explained solely by a reduction in food intake (FI). This study evaluated AM251, a CB1R inhibitor, on body weight (BW), FI, and 24-hr energy expenditure (EE) in a canine experimental model. **Methods:** 18 obese female beagles, age >2 yr were randomly assigned for 4 weeks to: 100% body weight maintenance-fed (BWMF) plus AM251 (2 mg/kg) group; 100% BWMF control group (C); or 70% BWMF food-restricted group (FR). Efficacy endpoints included EE (doubly-labeled water), body composition (dual-energy x-ray absorptiometry), and hematologic evaluations measured at baseline and Week 4; BW and FI were measured weekly. **Results:** Reductions from baseline BW at Week 4 were largest in the AM251 group (mean  $\pm$  SEM,  $7.9 \pm 1.9\%$ ) followed by the FR and C groups ( $5.9 \pm 1.1\%$  and  $1.3 \pm 0.5\%$ , respectively). At Week 4, both FR and AM251 groups showed similar FI reductions ( $p<0.05$  vs. baseline) compared to no change in the C group. The FR group showed a significant reduction in EE at Week 4 ( $p<0.01$  vs. baseline) compared with no change in C and AM251 groups. A significant difference in EE was observed between FR and AM251 groups at Week 4 ( $p<0.050$  for FR vs. AM251). There were no significant between-group differences in plasma levels of T3 and cortisol. **Summary:** Pharmacologic inhibition of CB1R in this dog model led to a significant reduction in BW. Weight loss appeared to be driven by a significant reduction in FI and in maintenance of 24-hr EE at pre-treatment/pre weight loss levels.

### 738-P

#### Sex-Associated Differences in Free Fatty Acid (FFA) Kinetics in Obese Adolescents With Insulin Resistance

Diane C. Adler-Wailes, Vipul Periwal, Asem H. Ali, Ayelet Spitzer, Abena Akomeah, Sheila M. Brady, Carson C. Chow, Jack A. Yanovski *Bethesda, MD*

**Background:** Adult studies have found sex-associated differences in insulin-mediated FFA flux related to body composition and resting energy expenditure (REE). However, sex-related differences in FFA kinetics have not been previously reported in obese, insulin-resistant adolescents. **Methods:** 159 subjects (age  $14.4 \pm 0.1$  y, BMI  $40.4 \pm 0.6$  kg/m<sup>2</sup>, 65% girls) underwent an insulin-modified frequently sampled intravenous glucose tolerance test; glucose, insulin, and FFA were measured. To estimate insulin-dependent FFA measures, including insulin dependent lipolysis rate ( $L_p$ ), insulin concentration required for 50% suppression of lipolysis (ED-50), and FFA clearance rate ( $C_p$ ), each subject's data were modeled assuming insulin suppresses lipolysis through one remote compartment that acts on both glucose and FFA.  $S_1$  was calculated using the Minimal Model. Fat mass (FM) and lean body mass (LBM) were also measured by air-displacement plethysmography and REE (indirect calorimetry). Sex effects for parameter estimates were tested with ANCOVA accounting for height, age, REE/LBM, and FM. **Results:** Girls and boys had similar FM ( $52.4 \pm 2.2$  vs.  $54.9 \pm 2.4$  kg,  $p=0.46$ ) and  $S_1$  ( $1.6 \times 10^{-4} \pm 1.5 \times 10^{-5}$  vs.  $1.3 \times 10^{-4} \pm 1.7 \times 10^{-5}$ ,  $p=0.41$ ). Girls had significantly lower LBM ( $p<0.05$ ) and REE ( $1882 \pm 28$  vs.  $2058 \pm 30$ ,

$p < 0.001$ ). There was a nonsignificant increase for girls in  $L_2$  ( $P = 0.08$ ). Girls had significantly higher ED-50 ( $40.5 \pm 1.6$  vs.  $35.4 \pm 1.8$ ,  $p < 0.05$ ) and  $C_i$  ( $0.105 \pm 0.01$  vs.  $0.089 \pm 0.01$ ,  $p < 0.04$ ). REE contributed significantly to ED-50 ( $p < 0.001$ ) whereas LBM predicted  $C_i$  ( $p < 0.005$ ). Conclusions: Girls trended towards having increased rate of insulin-dependent lipolysis compared to boys, greater ED-50, and more rapid plasma FFA clearance. These findings are consistent with the sex-associated differences in FFA kinetics reported in adults.

**739-P****Paradox Lost: Why Precise Control of Food Intake is Not Necessary For a Stable Body Weight**Carson C. Chow, Kevin D. Hall *Bethesda, MD*

Body weight change occurs when food intake and energy expenditure are imbalanced, and small persistent imbalances can accumulate to generate significant weight change. Yet adult human body weight is remarkably stable given the marked daily fluctuations of food intake and physical activity. This apparent paradox has bedeviled obesity researchers for more than three quarters of a century and the usual inference is that there must be an incredibly precise feedback control mechanism matching food intake to energy expenditure. Here, we show that a relatively imprecise intake control system is sufficient to maintain a stable body weight because the known dynamics of human weight change effectively damp large fluctuations of food intake. We use stochastic calculus applied to a simple mathematical model of human weight change and demonstrate that food intake variations of  $\sim 600$  kcal/d will maintain body weight to within  $\sim 1$  kg. We show that this result also holds true in a physiologically realistic computational model of human macronutrient metabolism. Our results imply that feedback control systems operating to regulate food intake in humans need not be as precise as previously believed.

**740-P****Energy Metabolism During an Extreme Weight Loss Program Involving Intense Daily Physical Activity**Nick D. Knuth *Bethesda, MD*; Darcy L. Johannsen *Baton Rouge, LA*; Robert Huizenga *Los Angeles, CA*; Eric Ravussin *Baton Rouge, LA*; Kevin D. Hall *Bethesda, MD*

We investigated energy balance dynamics during rapid weight loss in nine obese subjects (7 women, 2 men; BW:  $143.5 \pm 43.7$  kg, BMI:  $49.1 \pm 11.2$ ) taking part in "The Biggest Loser" television program. Subjects participated in vigorous physical activity for  $\sim 4$  h/d, 6 days per week in an isolated boot camp setting for  $\sim 93$  days with a modest reduction in energy intake. Exercise and diet regimens were continued at home until the final weigh-in at 30 weeks. A computational model of human metabolism was used to quantitatively integrate data on body composition, total energy expenditure (TEE), and resting metabolic rate (RMR). Model simulations predicted the average energy intake and physical activity underlying the observed weight losses. TEE measured by doubly labeled water increased from  $3733 \pm 1036$  kcal/d at baseline to  $4578 \pm 1045$  kcal/d at week 6. During the boot camp period subjects lost  $28 \pm 3\%$  of their initial body weight and computer simulations predicted an average energy intake of 1233 kcal/d and TEE of 4676 kcal/d with a physical activity expenditure of 2338 kcal/d. Total weight loss was  $43 \pm 9\%$  at 30 weeks and computer simulations predicted average energy intake increased to 1633 kcal/d and average TEE dropped to 3138 kcal/d as a result of a 50% decrease of physical activity at home. The final week TEE measurement was  $2909 \pm 548$  kcal/d. Our model of metabolic adaptation needed to be augmented to match the RMR data suggesting supra-linear increases of metabolic adaptation with greater decrements of energy intake.

**Integrative Physiology of Obesity****741-P****Glucocorticoid Antagonists Improve Insulin Sensitivity in Mice**Tomoko Bofelli *Stanford, CA*; Joseph K. Belanoff *Menlo Park, CA*; Philip Tsao *Stanford, CA*; Robin Clark *Menlo Park, CA*

Previous research has shown that CORT 108297, a member of the 1H-pyrazolo[3,4-g]hexahydro-isoquinoline class of selective glucocorticoid receptor antagonists, can improve insulin resistance caused by antipsychotic medications such as olanzapine (Belanoff, 2010). The goals of this study

were to test the efficacy of CORT 113083 and CORT 112716 and to confirm the efficacy of CORT 108297 for preventing changes in insulin sensitivity induced by a high fat and high sucrose diet. Ten week old, C57BL/6J, male mice were assigned to: 1) Vehicle, 2) CORT 113083 (80mg/kg/day), 3) CORT 112716 (80mg/kg/day), 4) CORT 108297 (80mg/kg/day) or , 5) Chow only. The high fat/high sucrose diet consisted of 60% fat calories and 20% sucrose supplemented with water ad libitum (D12492, Research Diets Inc.). Insulin sensitivity was measured at weekly intervals using the insulin suppression test. After a 4-hour fast, mice were injected i.p. with 300 $\mu$ L of saline containing insulin (1U/kg), glucose (1.3g/kg) and somatostatin (0.13mg/kg). Steady-state plasma glucose (SSPG) value was determined by the average blood glucose values at 60, 70 and 80 minutes after injection. At four weeks, groups assigned CORT 113083, CORT 112716, and CORT 108297 had significantly lower steady state plasma glucose levels than vehicle (all  $p < .05$ ). CORT 113083, CORT 112716, and CORT 108297, all selective glucocorticoid receptor antagonists, significantly improved insulin sensitivity in high fat/high sucrose fed mice. These findings add to a growing area of research suggesting that glucocorticoid receptor antagonists ultimately may be beneficial for treatment of insulin resistance often seen in obesity.

**742-P****Glucocorticoid Antagonist Attenuates Olanzapine-Induced Weight Gain in Rats**Joseph K. Belanoff, Robert L. Roe, Christine Blasey, Robin Clark *Menlo Park, CA*

Antipsychotic medications are consistently associated with weight gain and metabolic problems. Multiple publications have indicated that glucocorticoid antagonists are successful in blocking the weight gain caused by antipsychotic medications. Animal studies (Beebe, 2006), and randomized clinical trials in humans have shown that mifepristone can prevent and reverse weight gain caused by the commonly-used antipsychotics, olanzapine (Gross, 2009) and risperidone (Gross, 2010; *Obesity*, in press). Recently, a novel compound CORT 108297, with properties similar to mifepristone but without progesterone activity, was demonstrated to effectively mitigate olanzapine-induced weight gain in rats (Belanoff, 2010). The current study tested whether two novel compounds, similar in structure to CORT 108297, could prevent olanzapine-induced weight gain. Female Sprague-Dawley rats ( $n = 60$ ) were fed a normal chow diet. Animals were assigned ( $n = 10$  per group) to receive 18 days of one of the following treatments: vehicle, olanzapine (1.2 mg/kg), olanzapine + CORT 112716 (20mg/kg), olanzapine plus CORT 112716 (60mg/kg), olanzapine + CORT 113083 (20mg/kg), and olanzapine + CORT 113083 (60mg/kg). The groups exhibited significantly different amounts of body weight gain (time-by-treatment interaction,  $p < .00001$ ). The olanzapine group gained significant weight ( $m = +30$ ,  $sd = 12$ ,  $p < .00001$ ). Animals receiving O+11276 (60mg/kg) and animals receiving O+113086 (60mg/kg) gained significantly less weight than animals receiving olanzapine ( $p = .014$  and  $p = .038$  respectively). The novel compounds tested herein both significantly attenuated the weight gain induced by the antipsychotic medication olanzapine. The consistency of these findings is promising. Ultimately, this line of research could lead to discovery of novel treatments for the prevention and treatment of significant weight gain among persons using antipsychotic medications.

**743-P****What Modulates the Glut4 Expression in Skeletal Muscle After Sleeve Gastrectomy**Yong Wang, Jingang Liu *Shenyang, China*

Background: This study was designed to determine whether the improvement in insulin sensitivity is related to the phosphorylation of glut4 in skeletal muscles after sleeve gastrectomy, and what affect these changes. Methods: 30 GK rats were allocated into gastrectomy and control group. All survived rats were randomized into fasting gastrectomy group (FGG,  $n = 7$ ), fasting control group (FCG,  $n = 5$ ), no-fasting gastrectomy group (NFGG,  $n = 7$ ) and no-fasting control group (NFCG,  $n = 5$ ) 20 days later. All non-fasting rats received 2g/kg glucose through esophagus 30 minutes before sacrifice. Blood glucose and insulin concentrations, glut4 and insulin receptor expression in skeletal muscle, phosphorylation of glut4, IRS-1mRNA and IRS-2mRNA expression were measured. The structure of mitochondria in skeletal muscle was checked with transmission electron microscope. Results: Fasting Insulin concentrations

were  $1.584 \pm 0.211$  ng/ml,  $1.781 \pm 0.198$  ng/ml,  $2.13 \pm 0.203$  ng/ml and  $2.513 \pm 0.212$  ng/ml in FCG, NFCG, FGG and NFGG groups, respectively. There were no statistical differences between 4 groups in insulin receptor and glut4 expression. The pglut4 expression were  $1.24 \pm 0.11$ ,  $2.21 \pm 0.31$  (compared with FCG,  $P < 0.01$ ),  $3.35 \pm 0.26$  (compared with FCG,  $P < 0.01$ ) folds of FCG group, respectively. In NFCG, FGG and NFGG groups, the IRS-1mRNA expression were  $1.36 \pm 0.3$ ,  $1.24 \pm 0.31$  and  $1.71 \pm 0.23$  folds of FCG group, and the IRS-2mRNA expression were  $1.45 \pm 0.1$  (compared with FCG,  $P < 0.05$ ),  $1.58 \pm 0.21$ ,  $2.11 \pm 0.29$  (compared with NFCG,  $P < 0.05$ ) folds. No swelling of mitochondria could be found in FGG and NFGG groups. Conclusion: Sleeve gastrectomy is proved effective in modulating insulin secretion. The expression of glut4 and pglut4 were up-regulated after surgery, especially the expression of pglut4. Post-insulin receptor regulation might be an important role in treating diabetes after sleeve gastrectomy.

#### 744-P

##### The Role of Estrogen in Gender Differences in the Susceptibility to Obesity and Its Morbidities

Renee E. Stubbins, Valerie B. Holcomb, Jina Hong, Kyoko Kushiro, Nomeli P. Nuñez Austin, TX

Background: Obesity increases the risk of diabetes, cancer, and liver steatosis. The dysregulation of estrogen metabolism is associated with the above diseases. Here we explore the role estrogen plays in gender differences in obesity and its related morbidities. Methods: To determine the role of estrogen in gender differences in the susceptibility to obesity we used C57BL/6J mice (15/group): 1) males 2) nonovariectomized females 3) ovariectomized females and 4) ovariectomized females supplemented with estrogen, which were randomized to the following diets: 30% calorie-restricted, low-fat or high-fat diet. We measured weight gain, percent body fat, abdominal adipose tissue, and adipocyte size. Additionally, we assessed liver pathology, insulin sensitivity, and serum markers of inflammation. Results: Male mice were more susceptible to obesity than female mice. Removal of the ovaries eliminated the protection to obesity and estrogen supplementation restored this protection in females. In the low-fat and high-fat diet groups, male and ovariectomized female mice gained more abdominal adipose tissue due to increased adipocyte size compared to nonovariectomized female mice and ovariectomized female mice supplemented with estrogen. Moreover, males and ovariectomized females consuming the high-fat diet had significantly higher incidence of liver steatosis, insulin resistance, and inflammation. Conclusion: Male mice are more susceptible to the obesogenic effects of high fat diets compared to nonovariectomized female mice. In ovariectomized females, estrogen supplementation has a protective effect against obesity, insulin resistance, liver steatosis and inflammation. Manipulation of estrogen status in mice is a useful approach to understanding its effects on physiological traits underlying chronic diseases related to obesity.

#### 745-P

##### Preventing Cellular Obesity Changes and Target Organ Damage: The Heart By Ethanollic Gymnema Sylvestre in Murine Model of Obesity

Uma Bhandari, Vinay Kumar New Delhi, India

The International Obesity Task Force estimates that more than 300 million individuals worldwide are obese. Obesity plays a central role in the insulin resistance syndrome which is associated with hyperinsulinemia, hypertension, hyperlipidemia, type 2 diabetes mellitus, and an increased risk of atherosclerotic cardiovascular disease. Cardiomyocyte apoptosis seems to play a critical role in the development and progression of obesity. There is a significant positive correlation between mean dietary fat intake and the incidence of obesity and its related complications and risk factors. *Gymnema sylvestre* leaves extract (GSE) (Asclepiadaceae) has been used frequently in traditional Indian medicine for the treatment of diabetes. Adult male Wistar rats (150-200 g body wt), when subjected to orally fed high fat diet (20 gm/day) for a period of 28 days resulted in significant ( $P < 0.01$ ) increase in BMI, organ weights (heart, liver and kidney), visceral fat pad weight, cardiac caspase-3, cardiac DNA laddering (indicating apoptotic inter-nucleosomal DNA fragment) and lipid peroxides levels of heart and liver tissues of rats. Further, mean arterial blood pressure, heart

rate, serum leptin, insulin, LDH, LDL-C, total cholesterol, triglycerides and apolipoprotein-B levels were enhanced significantly whereas serum HDL-C and apolipoprotein-A1 levels, cardiac  $\text{Na}^+\text{K}^+$  ATPase, glutathione (GPx, GR, GST), catalase and SOD levels were significantly decreased. Furthermore, Treatment with standardized ethanolic GSE (200 mg/kg p.o.) for a period of 28 days resulted in significant reversal of above-mentioned changes in the obese Wistar rats. The present study reports for the first time significant antiobesity potential of GSE in murine model of obesity.

#### 746-P

##### Testosterone Effects on Direct Free Fatty Acid Storage Pathways in Men

Sylvia Santosa, Michael D. Jensen Rochester, MN

Background: Direct storage of circulating free fatty acid (FFA) may contribute to sex-associated differences in regional body fat distribution. This study aimed to elucidate the effects of testosterone on regional circulating FFA storage pathways in men. Methods: We studied 12 men undergoing  $>6$  mo androgen deprivation therapy (T-) and 13 age- and BMI-matched men with normal testosterone levels (T+). FFA storage rates were measured by combining a continuous infusion of [ $^{13}\text{C}$ ]palmitate and an IV bolus of [ $^{1-14}\text{C}$ ]palmitate followed 30 minutes later by abdominal and thigh subcutaneous adipose tissue (SAT) biopsies. Adipose tissue diacylglycerol acyltransferase (DGAT) and acyl-CoA synthetase (ACS) activity assays and CD36 protein content were measured. Results: FFA storage rates ( $\mu\text{mol kg fat}^{-1} \text{min}^{-1}$ ) were not significantly different between groups or depots. DGAT activity ( $\text{pmol mg AT lipid}^{-1} \text{min}^{-1}$ ) was greater ( $p = 0.02$ ) in abdominal vs. thigh SAT in T+ men, whereas ACS activity ( $\text{pmol mg AT lipid}^{-1} \text{min}^{-1}$ ) was greater ( $p < 0.05$ ) in thigh vs. abdominal SAT in T- men. Thigh ACS activity was also greater ( $p = 0.01$ ) in T- than in T+ men. No differences in CD36 content were noted between groups or depots. DGAT activity/1000 cells correlated ( $p < 0.05$ ) with thigh FFA storage rate/1000 cells in T+ men, whereas ACS activity correlated ( $p = 0.02$ ) with thigh FFA storage rate/1000 cells in T- men. Conclusion: Although we found no differences in direct FFA storage rates between groups, we did find differences in lipogenic protein activity. These differences indicate that regional FA storage may be regulated through different proteins in testosterone deficiency. Funding: NNCR-1UL1-RR024150, NIH-R01-DK45343, ADA-7-06-DCS-03. SS: NSERC, CDA

#### 747-P

##### Effect of Dietary Fiber Derived From Pulses or the Prebiotic Oligofructose on Satiety Hormone Secretion and Lipid Metabolism in Diet-Induced Obese Rats

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Background: The decline in dietary fiber intake has occurred alongside the increased prevalence of obesity and metabolic syndrome. Our objective was to determine the effect of diets enriched in pulse-derived ingredients, particularly fiber and starch, on satiety hormone secretion and lipid metabolism in diet-induced obese (DIO) rats. The prebiotic fiber, oligofructose, was used as a comparison. Methods: Adult, DIO Sprague-Dawley rats ( $n = 50$ ) were randomized to one of 5 diets for 6 wk: 1) control (C); 2) yellow pea flour (PFL, 33% wt/wt); 3) yellow pea starch (PS, 33% wt/wt); 4) yellow pea fiber (PF, 33% wt/wt containing 12% fiber); 5) oligofructose (OFS, 12% wt/wt). Outcome measures included body composition, satiety hormone levels, hepatic triglyceride (TG) content, and hepatic gene expression related to lipid metabolism. Results: C rats had higher body fat (%) than OFS and PFL ( $p < 0.01$ ). PFL rats had lower fasting leptin than C and PF rats ( $p < 0.05$ ). PF rats had lower glucose area under the curve (AUC) during the meal tolerance test than all other diets. OFS rats had higher peptide YY AUC than all other diets. PFL rats had lower GLP-1 AUC compared to C, PF and OFS. OFS rats had lower hepatic SREBP1c mRNA than PF and higher ACC mRNA than C and PF ( $p < 0.05$ ). PFL rats had lower TG content than PS. Conclusions: A diet containing pulse flour reduces weight gain and hepatic TG content but a diet enriched in pulse fiber is most favorable for reducing glucose excursion during a test meal. Funded by Alberta Pulse Growers, Agriculture & Food Council, Advanced Education & Technology.

## 748-P

**Decreased Niemann-Pick C1 Gene Dosage in a Mixed Genetic Mouse Strain Promotes Weight Gain and Metabolic Features Associated With Insulin Resistance**David Jelinek, Randall A. Heidenreich, William S. Garver, *Albuquerque, NM*

A recent genome-wide association study has revealed that the Niemann-Pick C1 (*NPC1*) gene is associated with early-onset weight gain in European populations. To further investigate this association, we used a candidate gene approach and performed a growth study using the BALB/cJ *Npc1* mouse model. In brief, *Npc1* homozygous normal (*Npc1<sup>+/+</sup>*) and *Npc1* heterozygous (*Npc1<sup>+/-</sup>*) mice were fed either a low-fat (10% kcal fat) or high-fat (45% kcal fat) diet for a period of 20 weeks. The results indicated that *Npc1<sup>+/-</sup>* mice, characterized by decreased *Npc1* gene dosage, had significantly increased weight gain at 13 weeks of age when fed a high-fat diet, consistent with a gene-diet interaction. We have extended these studies by interbreeding the BALB/cJ *Npc1* gene into the C57BL/6J mouse strain, which is susceptible to high-fat diet-induced weight gain and development of metabolic features associated with insulin resistance. The results demonstrated that decreased *Npc1* gene dosage in these mice was associated with weight gain and impaired glucose tolerance, whether the mice were fed a low-fat or high-fat diet. Moreover, mice fed a high-fat diet developed hepatic steatosis, adipocyte hypertrophy, and elevated levels of fasting plasma glucose, insulin, and leptin, consistent with metabolic features associated with insulin resistance. Therefore, decreased *Npc1* dosage present in this mixed genetic mouse strain was found to be particularly susceptible to high-fat diet-induced weight gain and development of metabolic features associated with insulin resistance, suggesting a previously unidentified and important role of human *NPC1* gene variants that may be present among certain populations.

## 749-P

**A Rat Model of the Lean Phenotype: High Daily Activity and Energy Expenditure, Regardless of Body Weight**Colleen M. Novak *Kent, OH*; Lauren G. Koch, Steven L. Britton *Ann Arbor, MI*

High daily physical activity is linked to leanness and high intrinsic aerobic endurance in both rats and humans. Here, we hypothesize that this leanness is due in part to heightened daily energy expenditure (EE), specifically energy expenditure of activity. Because body mass is the primary determinant of EE, accurately comparing EE between lean and obese individuals has continually hampered the ability to test this hypothesis. Here, we utilized a rat model of high and low intrinsic aerobic capacity derived through artificial selection; lean, high-capacity rats (HCR) are consistently more active compared to the low-capacity rats (LCR), which are prone to metabolic and cardiovascular disease. We measured EE in female HCR and LCR (n=13/group) which, unlike male HCR and LCR, overlap in body weight. The results consistently demonstrated that HCR have higher EE than LCR. This effect held when the rats were matched by body weight (n=9/group; within 4 g body weight), or by lean mass (n=8/group; within 7 g lean mass); in these cases, EE was higher in HCR than LCR by 8% and 13%, respectively. Daily physical activity was also higher in HCR than LCR in each subgroup of rats analyzed. Preliminary analyses suggest that the difference in daily EE was due to heightened resting as well as non-resting EE in HCR. Taken together, these results strongly suggest that energy expenditure of activity is in part responsible for the leanness seen in the high-endurance phenotype. Identifying the traits underlying this lean phenotype may be one key to countering obesity.

## 750-P

**Influence of a Rat Chromosome 1 Congenic on Renal and Obesity Phenotypes**Craig H. Warden, Rodrigo Gularte, Janis S. Fislser, Susan Hansen, Noreene Shibata, Juan E. Medrano, Judith S. Stern *Davis, CA*

Linkage mapping for renal disease traits in a backcross of [Brown Norway (BN) x Zucker (ZK)] x ZK identified a male specific quantitative trait locus (QTL) for urinary albumin excretion (UAE) on rat chromosome 1 (chr1). A congenic strain (ZK.BN-chr1) was produced containing 130 Mb of donor alleles from BN chr1 on ZK background. Linkage mapping was performed by crossing parents heterozygous for both the congenic donor region and ZK leptin receptor fatty mutation (*Lepr<sup>fa</sup>*). Males at 15 weeks were genotyped with sixteen microsatellite markers within the donor

region. Linkage analysis was performed including and excluding *Lepr<sup>fa</sup>* as an interactive covariate. Mapping results show two separate and highly significant QTL for both UAE and urinary albumin/creatinine ratio (ACR). The proximal peak was located at 190 Mb (LOD>15), whereas the distal peak was at 260 Mb (LOD=13). Blood urea nitrogen had a significant QTL at 190 Mb (LOD>10) but was baseline at 260 Mb. Serum triglyceride (TG) levels showed both proximal and distal QTLs (LODs=6,10). Mesenteric and gonadal fat weights had a significant QTL from 180 – 190 Mb (LOD=8). We confirm the published ACR QTL and demonstrate that renal function and fat depot weights have co-localized QTL in the middle portion, and ACR and TG in the distal portion, of the ZK.BN-chr1 congenic. Significant interactions were observed between the *Lepr* genotype and QTL for urine volume, UAE and liver and kidney weights.

## 751-P

**Role of Leptin in Fever and Pyrogenic Signalling to Lipopolysaccharide in Obese Rats**Joanna Pohl, Gokce Somay *Verdun, Canada*; Claudia Frate, Barbara Woodside *Montreal, Canada*; Giamal Luheshi *Verdun, Canada*

Introduction: Leptin was shown to modulate the fever response to lipopolysaccharide (LPS). Leptin may also affect pyrogenic mechanisms by activating microglia to release IL-1 $\beta$ . We have previously reported that obese rats exhibit a greater fever response than lean controls, accompanied by increased circulating leptin levels. Here we investigated if leptin changes the inflammatory response of obese rats, by fasting (Exp.1) or neutralizing leptin by administering leptin specific anti-serum (LAS) (Exp. 2), and measuring fever and pyrogenic signalling in the hypothalamus. Methods: Male Wistar rats (250-300g) were given free access to a liquid diet supplement in addition to standard laboratory chow, until their body weight exceeded by 15% that of controls. To reduce endogenous leptin levels, rats were either fasted for 24h prior to LPS injection (Exp.1) or were injected with LAS (Exp. 2). Core body temperature was measured using remote radio-biotelemetry (TA10TA-F40, Data Sciences). Expression of IL-1 $\beta$  and CD11b, were quantified in the hypothalamus in rats of Exp.1. Results: Both fasting and administration of LAS attenuated the fever response of obese rats (p < 0.05) but LAS treatment had a greater effect. Fasting did not change expression for either IL-1 $\beta$  or CD11b (p > 0.05). Conclusion: These data suggest that leptin contributes to the enhanced fever response. Although IL-1 $\beta$  and CD11b expression was not changed, their levels were only analyzed in Exp.1. Given that the attenuation in fever in Exp.1 was more modest, LAS may have a greater effect. Results of Exp. 2 are presently being analyzed.

## 752-P

**Dark-Cycle Feeding and Meal Pattern Analysis in Rats Following Peripheral Administration of the Novel Amylin-Mimetic Peptide Divalintide**Julie K. Wilson, David Parkes, Christine M. Mack *San Diego, CA*

The current experiments examined dark-cycle feeding and meal patterns in rats treated with davalintide (DAV), a novel, second-generation peptide analog of rat amylin possessing a prolonged duration of action over the native hormone to reduce food intake. Male Sprague-Dawley rats (414-541 g, 32-45% kcal fat diet) received an IP injection of peptide (n=5-8/group) at lights off and food consumption was measured for 20-24 h via an automated food intake recording system. Results showed amylin (100  $\mu$ g/kg) to suppress food intake at hours 1, 2 and 4-6, compared to vehicle (p<0.05). A second experiment showed a two-fold lower dose of DAV (50  $\mu$ g/kg) to decrease food intake for up to 23 h post injection; this resulted in decreased body weight gain following 4 nights of treatment (DAV= -8.2 $\pm$ 1.5 g, vehicle=+1.6 $\pm$ 1.2 g, vehicle-corrected change=2.1%, p<0.05). In experiment three, meal pattern analysis showed DAV (5, 10 and 20  $\mu$ g/kg) to decrease meal size compared to vehicle (first meal) at all doses (vehicle=4.5 $\pm$ 0.7 g; 5  $\mu$ g/kg=1.9 $\pm$ 0.5 g; 10  $\mu$ g/kg=2.4 $\pm$ 0.5 g; 20  $\mu$ g/kg=2.2 $\pm$ 0.3 g, p<0.05 for each). DAV at 20  $\mu$ g/kg also increased latency to eat (vehicle=8.5 $\pm$ 5.4 min; DAV=173.7 $\pm$ 51.6 min, p<0.05). There were non-significant trends for DAV to increase intermeal interval (IMI), decrease meal duration and increase the satiety ratio (IMI/meal size). 24-h food intake was dose-dependently decreased, with significant reductions at all doses (vehicle= 18 $\pm$ 0.9 g; 5  $\mu$ g/kg=15 $\pm$ 1.5 g; 10  $\mu$ g/kg=14 $\pm$ 0.7 g; 20  $\mu$ g/kg=13 $\pm$ 0.9 g, p<0.05 for each). These data show DAV to reduce food intake in part through mechanisms involved in meal termination.

## 753-P

**Effects of an Arachidonic Acid-Docosahexaenoic Acid Mixture on the Development of Obesity and Its Related Disorders**

Lucien F. Harthoorn *Nijmegen, Netherlands*; Zeina E. Jouni *Evansville, IN*; Ric Van Tol *Nijmegen, Netherlands*; Lars Verschuren, Robert Kleemann, Teake Kooistra *Leiden, Netherlands*

Arachidonic acid (ARA) and docosahexaenoic acid (DHA) have been proven to support brain development and vision and their dietary supplementation is therefore considered to be health beneficial, especially during early life stages. This study addresses whether ARA-DHA supplementation, at relatively low amounts, is effective in reducing the development of obesity and its related disorders. This was tested in ApoE3L-transgenic mice, a humanized animal model for hyperlipidemia with mild obesity and insulin resistance, which were fed a high-fat/high-carbohydrate (HFHC) diet. ApoE3L-mice were fed *ad libitum* with a HFHC-diet (28% fats, 42% carbohydrates) in the absence or presence of 0.129wt% ARA and 0.088wt% DHA. Food intake, body weight, plasma cholesterol, plasma triglycerides and fasting glucose and insulin were measured during a 16-weeks feeding period. At the end of the experiment, plasma levels of HDL-, LDL-, VLDL-cholesterol and fat tissue and liver weights were determined. Throughout the feeding period, mice that were fed the ARA-DHA supplemented HFHC-diet gained less body weight in comparison to the control group with the HFHC-diet only. ARA-DHA supplementation also lowered plasma cholesterol and fasting glucose levels. At the end of the experiment, ARA-DHA supplemented mice had a reduced relative liver weight and an increased HDL/LDL-ratio as compared to their controls. No effects of ARA-DHA supplementation were found on food intake, insulin levels, and fat tissue weights. This study shows that in a HFHC-dietary context, supplementation of ARA and DHA in relatively low amounts has health benefits on body weight, plasma cholesterol, plasma glucose levels and liver health.

## 754-P

**Weight Loss in Obese Subjects Reduces the New Macrophage Derived Risk Factor, Soluble CD163, in the Circulation**

Bjorn Richelsen, Tore Christiansen, Jens Bruun, Holger Moller *Aarhus, Denmark*

Activation of adipose tissue macrophages with concomitant low-grade inflammation is believed to play a central role in the development of type 2 diabetes and other metabolic diseases. We tested whether a new macrophage biomarker, soluble CD163 (sCD163), was affected by diet-induced weight loss and exercise in obese subjects. Material and Methods: 79 obese women and men were randomized in three groups and treated for 12 weeks with 1) exercise-only (EXO), 2) Diet-induced weight loss (DIO) for 8 weeks VLED followed with 4 weeks weight loss maintenance diet, and 3) the combined group with both exercise and diet-induced weight loss (DEX). Serum levels of sCD163 were determined by an in-house sandwich ELISA (Dade Behring). Adiponectin and inflammatory markers (Luminex) were determined before and at the end of the intervention. Results: Weight loss was after the 12 weeks 3.5 kg (EXO) and 12 kg in both DIO and DEX. HOMA decreased in all three groups ( $p < 0.05$  in the DIO and DEX groups). Exercise alone had no effects on sCD163. In the DIO and DEX groups sCD163 was significantly reduced by 25% ( $p < 0.05$ ). Changes in sCD163 was positive correlated with changes in body weight ( $r = 0.44$ ,  $p < 0.01$ ) and negatively correlated with changes in adiponectin ( $r = 0.38$ ,  $p < 0.01$ ). Conclusion: In obese subjects sCD163 is reduced in association with larger weight losses. Exercise training for 12 weeks resulting in enhanced  $VO_{2max}$  and a weight loss of 3.5 kg had no effect on circulating sCD163. sCD163 is rather closely related to changes in adiponectin.

## 755-P

**Involvement of L-Arginine/NO Pathways on the Vascular Adaptive Response of Obese Rats**

Thiago Bruder Nascimento, Dijon Henrique Salom Campos, Antonio Carlos Cicogna, Sandra Cordellini *Botucatu, Brazil*

Background: Relationship among vascular alterations, hypertension and obesity is well-known, but its causes are still poorly understood. The aim was to investigate the involvement of L-arginine/nitric oxide pathway on the vascular response of diet-obese rats. Methods: Male Wistar rats were separated into control (C, n=8) and obese (O, n=8) groups. Control received

a standard rat chow while obese received a high-fat diet (4 flavors: vanilla, cheese, chocolate and bacon) for 15 weeks. The body weight (BW) and blood pressure (BP) were measured once a week. After 15 weeks, the rats were killed and the index of adiposity (IA) was determined as follows: [epididymal fat+retroperitoneal fat+visceral fat]/[total body weight-sum of all adipose depots] $\times 100$ . Concentration-response curves to noradrenaline (NA) were obtained in the absence and presence of acute inhibition of nitric oxide synthase (L-NAME,  $3 \times 10^{-4}$  M) in intact and denuded thoracic aorta of C and O rats. Results: [Final BW (g): C  $433.5 \pm 40.3$ ; O  $498.4 \pm 38.3^*$ . Final BP (mmHg): C  $121.0 \pm 7.5$ ; O  $128.0 \pm 4.1$ . IA (%): C  $3.9 \pm 1.1$ ; O  $6.8 \pm 1.9^*$ . Maximum response to NA in intact aorta (g of tension): C  $2.8 \pm 0.2$ ; O  $1.8 \pm 0.6^*$ ; C/L-NAME  $4.3 \pm 0.4^{**}$ ; O/L-NAME  $3.9 \pm 0.2^{**}$ ; \* $P < 0.05$  related to control, \*\* $P < 0.05$  related to absence of L-NAME]. None of the procedures altered the response to NA in denuded aorta. Conclusion: Diet-induced obesity determines hyperactivation of the endothelial L-arginine/NO pathway that may counterbalance changes in arterial blood pressure of obese rats. Support: FAPESP

## 756-P

**Modest Hyperglycemia Prevents Interstitial Dispersion of Injected Insulin**

Cathryn M. Kolka, Ana Valeria Barros de Castro, Erlinda L. Kirkman, Richard N. Bergman *Los Angeles, CA*

Insulin injected directly into skeletal muscle diffuses rapidly throughout the interstitial space to cause glucose uptake, but not in fat-fed dogs. The observed hyperglycemia in fat-fed dogs during anesthesia may inhibit insulin access to muscle cells, rather than plasma lipid changes. Here we asked whether interstitial insulin diffusion is reduced in modest hyperglycemia under anesthesia. Normoglycemic (100mg/dl) and moderately hyperglycemic (120mg/dl) clamps with basal insulin replacement were performed under anesthesia. Five sequential doses of insulin (0.3-3U) were injected into the vastus medialis of one hindlimb (INJ); the non-injected contralateral limb (NINJ) served as a control. Femoral artery and vein plasma samples were analyzed for insulin content. As a surrogate for interstitial insulin levels, lymph vessels exiting the hind leg were also catheterized, and lymph samples were analyzed. As previously reported, intramuscular insulin injection caused interstitial (lymph) insulin to increase above NINJ in normoglycemic animals. This increase was not observed in moderately hyperglycemic animals. Insulin-mediated glucose uptake observed in normoglycemic controls was not observed in hyperglycemia. Modest hyperglycemia caused a failure of intra-muscularly injected insulin to diffuse through the interstitial space and failed to stimulate glucose uptake, compared to normoglycemic animals. Hyperglycemia prevents the appearance of injected insulin in the interstitial space, thus reducing binding to myocytes and contributing to insulin resistance.

## 757-P

**Ghrelin Concentrations in Response to Short-Term Overfeeding in Normal-Weight, Overweight, and Obese Men**

Kristina L. Sheridan, Farrell Cahill *Logy Bay, Canada*; Edward Randell, Sudesh Vasdev *St. John's, Canada*; Guang Sun *St. John's, Canada*

Ghrelin is a 28 amino acid peptide, and an endogenous ligand of the growth hormone receptor. It is the only gut hormone that is a proven orexigen, stimulating the appetite, increasing food intake, and inducing a positive energy balance. The development of obesity is a chronic positive energy balance. How gut hormones including ghrelin response to positive energy challenge could potentially a risk factor to obesity. The present study was designed to investigate the response of serum ghrelin to a 7-day overfeeding protocol (70% above normal caloric intake). A total of 72 men ( $\geq 3^{rd}$  generation Newfoundland) participated in this study. The hypercaloric diet was 70% above normal energy requirement. Baseline energy requirement evaluated using the Willet Frequent Food Questionnaire and three 24-hour recalls. Body composition was measured by BMI and dual energy X-ray absorptiometry (DXA). Fasting glucose, insulin, insulin resistance and beta cell function evaluated by the Homeostasis Model Analysis (HOMA-IR, HOMA- $\beta$ ), total cholesterol, HDL-cholesterol and LDL-cholesterol were measured as well. Serum ghrelin concentration, to our surprise, was significantly increased after the 7-day positive energy intervention. Further analysis by stratifying the subjects by tertile method, it was discovered that the significant increase of ghrelin was in the medium BMI group (middle 33%).

No significant change was observed between ghrelin and all other phenotypes at baseline or the changes in response to overfeeding. Further study using larger study regarding to the mechanism causing the differences of ghrelin response between BMI groups is warranted.

**758-P****The Attenuating Effect of a High Resistant Starch Diet During Pregnancy and Lactation on the Rate of Weight Gain of the Offspring Depends on Sex and Post-Weaning Diet Composition**

Alfred Aziz, Laura Kenney, Benoit Goulet, Krystle Talbot *Ottawa, Canada*

Diets high in resistant starch (RS) have been reported to reduce body weight in animal models. This study tested the hypothesis that a diet high in RS (10% by weight, HRS) fed to female Wistar breeders during pregnancy and lactation would reduce body weight in the offspring compared to an isoenergetic diet low in RS (0% RS; LRS). Female breeders were adapted to the experimental diets for 3 weeks during which both groups gained similar amount of weight and had similar glucose tolerance. There were no significant differences in pregnancy outcomes measures. At weaning, males and females (n=10-11 group) were segregated and given free access to either an AIN-93G (CTR) diet or a high fat, high energy diet (HFE) for 12 weeks. Body weight and food intake measurements were recorded weekly. At 15 weeks of age, the rats were euthanized and blood and tissues were collected. There were significant interactions between the maternal diet and time on body weight: in males, the rate of weight gain of HRS/CTR was lower than that of LRS/CTR ( $P < 0.05$ ), whereas in females, this effect of the HRS diet was observed with the HFE postweaning diet ( $P < 0.05$ ). Food intake tended to be lower in these groups, but not significantly. However, fat pad weights were similar regardless of the maternal diet. Current analyses are exploring plausible mechanisms involved in the regulation of energy balance. We conclude that a maternal diet high in RS might impart protective effects against weight gain in the offspring.

**759-P****Duration of High Fat Feeding Is Positively Correlated with Subsequent Chow Intake in C57BL/6 Mice: The Food Intake Ratchet Effect**

Juen Guo, Michael Dore, Carson C. Chow, Kevin D. Hall *Bethesda, MD*

Does a period of overeating lead to an upwards adjustment of habitual food intake? To investigate this question, we measured chow intake in 3-month-old male C57BL/6 mice following exposure to a high fat diet for varying durations. Specifically, singly housed mice were given *ad libitum* access to a high fat diet (5.45 kcal/g with 59% energy from fat) for either 0, 4, 7, 16, or 20 weeks and were then switched back to *ad libitum* chow for at least 12 weeks (3.79 kcal/g with 12% energy from fat). We found that the average energy intake over the last 9 weeks on the chow diet was positively correlated to the duration of prior high fat feeding. After correcting for the initial body weight, every week on the high fat diet led to a subsequent increase of chow intake by  $0.11 \pm 0.02$  kcal/d ( $r = 0.9$ ;  $P < 0.001$ ). These data suggest that a past history of overeating can lead to an upwards adjustment of food intake that acts as a ratchet inhibiting the return to a normal weight. Thus, diet history is an important contributor to the regulation of food intake in mice.

**760-P****A Human Virus Improves Diabetes**

Rashmi Krishnapuram, Emily J. Dhurandhar, Olga Dubuisson, Heather Kirk-Ballard, Sudip Bajpeyi *Baton Rouge, LA*; Nancy Butte *Houston, TX*; William Johnson, Meghan McGlone *Baton Rouge, LA*; Gregory Reinhart *Dayton, OH*; Tuomo Rankinen, Claude Bouchard, William T. Cefalu, Jianping Ye *Baton Rouge, LA*; Ronald Javier *Houston, TX*; Aamir Zuberi, Nikhil V. Dhurandhar *Baton Rouge, LA*

**Background:** A single inoculation of mice with Ad36, a human adenovirus, lastingly improved high fat diet-induced-diabetes (*DID*), while Ad2, another human adenovirus did not. **Objective:** To determine if Ad36 could be used as a tool to reveal novel pathways for improving dysglycemia in humans. **Approach:** Study 1: To understand the mechanism, we compared protein or mRNA abundance of over 60 proteins obtained from adipose tissue, skeletal muscle and livers of *DID* mice, that were infected with Ad36, Ad2, or Mock infected 20-wk earlier. Based on our results, we postulate the following working model for the anti-diabetic action of Ad36 in mice. Ad36 upregulates glucose uptake in skeletal

muscle and adipose tissue, via insulin-independent, but Ras-dependent, and PI3K (phosphatidylinositol 3-kinase) mediated upregulation of Glut4 and Glut1 transporters. In the liver, Ad36 reduces Glut2-mediated glucose output, increases glycogen and reduces lipid storage. Furthermore, Ad36 robustly increases adiponectin, which improves glycemic control via AMPK (AMP-activated protein kinase) activation in skeletal muscle and liver. Collectively, this improves dysglycemia in mice. Study 2: We tested if humans who were naturally infected with Ad36, have a better glycemic profile. Remarkably, natural Ad36 infection was associated with significantly better insulin sensitivity adjusted for age, sex, race and adiposity, both, in adults (n=671) and children (n=588). **Conclusion:** Considering that insulin signaling is often impaired in obesity or diabetes, the insulin-signaling independent glucose disposal by Ad36 may provide a particularly useful template for developing novel anti-diabetic drug targets, of relevance to humans. **Funding:** ADA-1-09-IN-13, The Mathile Institute.

**761-P****Lean Obesity Resistant Rats Have Fewer Physiological Markers of Aging Compared to Obese Sprague-Dawley Rats**

Jennifer A. Teske, Charles J. Billington, Catherine M. Kotz *Minneapolis, MN*

Age-related declines in physical activity parallel adiposity gain and presence of frailty and limited mobility in humans. We've shown that obesity resistant rats (OR) have less fat mass, more fat-free mass/body weight and maintain elevated physical activity compared to Sprague-Dawley (SD) rats from 1-19 months of age. This suggests that physical activity contributes to reduced adiposity gain during aging and implicates 'obesity resistance' as marker of aging well. Given that frailty and limited mobility are common with aged humans, we determined whether these markers of aging were present in this rodent model of obesity. Markers for frailty and limited mobility including distance traveled, movement velocity, movement bouts initiated were measured in OR and SD rats monthly for 18 months. Distance traveled, movement bouts, velocity and the distance traveled per movement bout decreased with age in both groups. OR rats traveled significantly further ( $p < .02$  at each month excluding 14-mo.) and initiated significantly more movement bouts at 2, 7, 9, 10 and 17-mo. of age ( $p < .05$  for all comparisons). Distance traveled per bout was significantly greater in OR rats at each measurement ( $p < .02$  at each month). Velocity was similar between groups through out 18 months, however, the decline in velocity from 1-18 months was less in OR rats ( $p = .0595$ ). These data suggest that OR rats age better with less limited mobility and frailty indicated by moving more per bout and a lower decline in velocity. The obesity resistant rat appears to be promising for aging research.

**762-P****Peptide YY (PYY) Responses to a 7-Day Positive Energy Challenge in Normal-Weight, Overweight, and Obese Young Men**

Farrell Cahill, Kristina L. Sheridan *Logy Bay, Canada*; Edward Randell, Sudesh Vasdev, Guang Sun *St. John's, Canada*

Gut hormones are important factors affecting food intake and the maintenance of energy homeostasis through gut-brain communication. Peptide YY (PYY), a linear 36amino acid, inhibits appetite and has been linked to the development of obesity. Our study was to investigate the relationship between PYY and obesity related phenotypes before and after a 7-day overfeeding protocol (70% above normal energy requirement). The study recruited 72 participants. The PYY concentration was significantly increased after the 7-day positive energy challenge ( $118.3\text{pg/ml} \pm 57.8$  to  $135.8\text{pg/ml} \pm 70.1$ ,  $p = 0.010$ ). However, no significant differences of serum PYY between normal weight, overweight and obese subjects based on BMI or Body Fat Percentage (%BF) measured by DXA. We analyzed the potential relationship between serum PYY before and after overfeeding and the PYY changes with baseline energy requirement measured by the Willet Frequent Food Questionnaire and three 24hr recalls, weight, BMI, %BF, waist circumference, glucose, insulin, insulin resistance and beta cell function evaluated by the Homeostasis Model Analysis (HOMA-IR, HOMA- $\beta$ ), total cholesterol, HDL, LDL. No significant correlation was found after controlling for age and %BF or BMI. The positive energy challenge was overwhelmingly strong and induced significant change in body composition related phenotypes, negative changes in lipids and insulin resistance in the entire cohort. To our knowledge, this is the first study on the regulation of PYY by positive energy challenge. The increase in PYY, likely a protective response to overfeeding, suggests its usefulness in the prevention/treatment of human obesity

**763-P****ZGN-201, a Methionine Aminopeptidase 2 (MetAP2) Inhibitor, Reduces Body Weight (BW) and Normalizes Glucose Tolerance in Overweight Dogs**

Thomas E. Hughes, James E. Vath *Cambridge, MA*; Melanie F. Scott, Joshua D. Roop, Jon R. Hastings, Phil E. Williams, Doss W. Neal, Erik R. Nass, Alan D. Cherrington *Nashville, TN*

MetAP2 inhibitor treatment reduces BW and food intake (FI) in obese mice by stimulating fat metabolism; however efficacy has not been established in non-rodent species. Feeding with a high-fat high-fructose (HFF) diet in dogs has been observed to induce weight gain and hepatic insulin resistance, reducing liver glucose extraction and causing glucose intolerance. We evaluated the effects of 8wk daily oral treatment with ZGN-201 on BW and metabolic parameters in 6 overweight dogs (3 HFF and 3 chow-fed (OWC)). The study included three phases – pretreatment (PT: 4wks), treatment (ZGNTx: 8wks), and washout (WO: 4-11 wks). FI, BW, clinical chemistry, beta-hydroxybutyrate (BHB), and glycerol were assessed weekly. Oral glucose tolerance tests (OGTT, 0.9 g/kg initial BW) were performed at the end of PT, ZGNTx, and WO. HFF dogs treated with ZGN lost 81% of excess BW. Treatment in OWC dogs inhibited weight gain. Following washout, HFF dogs regained 34% of the lost weight by 4wks WO, and weight stabilized with 50% of weight loss maintained after 11wks of WO. ZGN-201 reduced FI in HFF dogs by 29%, but by only 9% in OWC dogs. During treatment glycerol levels increased, reflecting enhanced lipolysis. BHB levels, reflecting fat oxidation, increased in HFF only. BHB and glycerol reverted to baseline after the washout period. ZGN-201 treatment reduced OGTT plasma glucose excursions, despite a 32% reduction in insulin secretion. After WO, the improvement in plasma glucose was completely reversed. These results suggest that MetAP2 inhibitor treatment improves glycemic control and reduces BW, which appears to be, in part, durable.

**764-P****Melatonin Treatment Along With a Hyperlipidic Diet Modifies 24 h. Variations of Pituitary Hormone Secretion**

Vanesa Jimenez-Ortega, Judith Rios-Lugo, Pilar Cano Barquilla, Ana Isabel Esquifino Parras, Pilar Fernandez-Mateos *Madrid, Spain*

Obesity is associated with a number of changes in basal values of pituitary hormones. Previous data from our group have shown that obesity also modifies the circadian secretory patterns of several pituitary hormones. The aim of the present work was to analyze if melatonin treatment (30 micrograms/mL) along with the hyperlipidic diet prevents the observed changes in obese rats. The secretory patterns of PRL, GH and TSH will be evaluated through a Luminex X- MAP Technology. Plasma prolactin levels were higher during the dark phase of the photoperiod in control animals. Melatonin treatment markedly increased plasma PRL levels during the light phase of the photoperiod and decreased it during the dark phase. Obesity markedly increased plasma PRL levels around the clock. Melatonin treatment partially normalized PRL level during the dark phase of the photoperiod. Melatonin treatment shift delayed the maximal values of GH from 17:00 h (controls) to 05:00h. Besides melatonin treatment did not modify the reduced plasma GH pattern observed in obese rats vs. controls. Melatonin treatment shift advanced the TSH peak from 05:00 h (controls) to 13:00 h. Obesity decreased plasma TSH levels and shift advanced its peak to 13:00 h. Melatonin treatment did not modify the TSH pattern described in obese animals. Melatonin partially prevents the changes observed in the secretory pattern of prolactin of obese rats but did not prevent those effects on GH and TSH secretory patterns.

**765-P****Pre-Operative Diabetes Is Associated With Poor Weight Loss Outcomes Following Roux-en-Y Gastric Bypass Surgery**

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Background: Identification of preoperative predictors of weight loss after Roux-en-Y gastric bypass (RYGB) surgery may lead to better clinical management. Few clinical variables have been found to predict weight outcomes following RYGB. Methods: Caucasian patients with a BMI greater than 35 kg/m<sup>2</sup> who underwent primary RYGB were included in the analysis. An analysis of available data on more than 200 clinical variables related to medication use, co-morbidities, and baseline laboratory and survey data was

performed to determine whether any differences present between the 150 patients who lost the most weight and the 150 patients who lost the least. Chi-square tests and Wilcoxon Rank sum tests were used after a Bonferroni correction. Results: A total of 1001 patients (80% female) with a mean age of 46.5 years and a mean initial BMI of 50.2 mg/kg were studied. The diagnosis of diabetes was almost twice as frequent in patients who lost the least weight ( $p < 0.0001$ ). Initial weight, BMI, excess body weight, and waist circumference were also statistically higher in patients who lost the least weight ( $p < 0.0001$ ), although the differences were likely not clinically significant in patients of this BMI range. Post-operatively, the percentage of patients with pre-operative diabetes that had a hemoglobin A1c over 6.5% was approximately 2-fold higher in the group who lost the least weight. Conclusions: A pre-operative diagnosis of diabetes and post-operative elevation of hemoglobin A1C levels were more prevalent in those patients with the poorest weight loss outcomes following RYGB surgery.

**766-P****Cold Exposure Methodology for Investigating Brown Adipose Tissue Activation in Humans**

Denis P. Blondin *Ottawa, Canada*; Veronique Ouellet *Quebec, Canada*; Andre Carpentier *Sherbrooke, Canada*; Denis Richard *Quebec, Canada*; Eric Turcotte *Sherbrooke, Canada*; Francois Haman *Ottawa, Canada*

Recent investigations have indicated that brown adipose tissue (BAT) can exist in substantial amount in adult humans. This observation has renewed the interest for BAT as well as for the role of adaptive thermogenesis in energy balance regulation. While the prevalence of BAT and its amount in adult humans are becoming clearer, much work remains to better understand BAT metabolism and thermogenic capacity. The purpose of this study was to develop a highly reproducible cold exposure protocol sufficient to stimulate BAT activity without quantitatively inducing substantial shivering activity. Working from previously reported changes in thermogenic rate and muscle activity in non-cold acclimatized men, subjects were exposed to the cold using a liquid-conditioned garment perfused with 18°C water for 3 hours during positron emission tomography coupled to computed tomography (PET/CT). Results indicate that thermal and metabolic responses were well maintained between trials. This cold exposure condition was compensable resulting in a ~3°C decrease in mean skin temperature without any change in core temperature. Total heat production rate increased by ~1.5-fold whereas shivering intensity in 4 major muscles remained extremely low at 1.5% of maximal voluntary contraction. Even though this cold exposure intensity was mild, it was sufficient to produce a 30% elevation in plasma cortisol and a significant activation of BAT activity as determined by <sup>18</sup>F-fluorodeoxyglucose PET/CT. We conclude that this methodology provides highly reproducible, well-controlled conditions to investigate BAT metabolism using PET/CT in cold exposed adult humans.

**767-P****Body Fat Distribution of the FHH-Chr N BN Chromosome Substitution Rat Strain Set**

Danielle R. Reed, Fujiko F. Duke, Matthew R. Rosazza, Laura K. Alarcon, Michael G. Tordoff *Philadelphia, PA*

We compared the amount and distribution of body fat in a set of FHH-Chr N BN chromosome substitution strains (CSSs). For these strains, a whole chromosome from the Brown Norway (BN) strain has been introgressed into the Fawn Hooded Hypertensive (FHH) host strain. Male rats from the parental strains and each of the 22 CSSs were fed AIN-76A diet until they were 330-370 days old, when we measured the weights of their gonadal, retroperitoneal, mesenteric, femoral, subscapular and pericardial adipose depots, as well as their body weights and lengths. Total body fat was defined as the weight of all dissectible depots, adjusted by regression methods for body length and weight. Body fat distribution was defined as (gonadal + retroperitoneal + mesenteric depot weights)/the weight of all dissectible fat. QTLs were identified using a general linear model followed by post-hoc tests between each CSS and the host strain (FHH). For total body fat, QTLs were found on Chr 1, 9, 14, 15, 18, 19 and X; for body fat distribution, QTLs were found on Chr 1, 2, 5, 12, 13 and 18. CSSs are useful for genetic studies and offer advantages for fine mapping and congenic construction, procedures aimed at identifying the genes underpinning QTLs. [Supported by NIH DC-10149 to MGT and NIH DK-58797 to DRR]

## 768-P

**Adipose Tissue of Offspring of Diabetic Mothers Has Increased Capacity to Glucose Uptake and Lipid Storage**

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Gestational diabetes causes fetal anomalies. Macrosomia or neonatal obesity is very common in gestational diabetes. Experimental models of diabetes showed damage in maternal and fetal lipid metabolism. Here, we evaluated in rats the repercussions of maternal diabetes on epididymal (EP) adipose tissue (AT) metabolism of offsprings. The offspring of diabetic mothers (ODM) were killed at 12 weeks of age, the serum was collected and EP fat was excised, weighed and adipocytes were isolated for biological tests (glucose uptake, oxidation and incorporation into lipids). Adipose tissue was frozen in liquid nitrogen for later measurement of protein by Western Blotting. The ODM group weighed more than control ( $319.8 \pm 13.25$  g vs.  $269.8 \pm 3.81$  g,  $p < 0.05$ ), and EP fat pad weight was 22% and the EP adipocyte diameter, 11% higher than controls ( $p < 0.05$ ). The ODM epididymal adipocytes showed higher basal (147%,  $p < 0.01$ ) and insulin-stimulated (120%,  $p < 0.05$ ) rates of [ $^3$ H]-2DG uptake than controls. The same happened to the D-[U- $^{14}$ C]-glucose incorporation into lipids [basal (Bs) and insulin-stimulated (Mx) (78% increase in Bs and Mx,  $p < 0.05$ ) and to the ability to oxidize carbohydrate into  $^{14}$ CO $_2$  (77% increase in Bs and 68% increase in Mx,  $p < 0.05$ ). The ODM group had a significantly ( $p < 0.05$ ) higher expression of Glut 4 (54%,  $n=4$ ), IR $\beta$  (100%,  $n=4$ ), ACC (190%,  $n=4$ ) and Perilipin A and B (50%,  $n=4$ ) than control in epididymal AT. In conclusion, the offspring from diabetic mothers showed a greater ability for storing lipids and became obese. Granted by *National Council of Scientific and Technologic Development (CNPq)*

## 769-P

**Estimating Hepatic Glucokinase Activity From the FSGIT Using a Novel Working Model of Lactate Metabolism**

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The Frequently Sampled Intravenous Glucose Tolerance Test (FSGIT) protocol is a widely used for the estimation of key glucose metabolic indices including insulin sensitivity ( $S_I$ ), glucose effectiveness ( $S_g$ ) and acute insulin response to glucose (AIR $_g$ ). It is often of interest to evaluate liver function separate from peripheral insulin sensitivity. Specifically, it has been shown that glucokinase (GK) plays a critical role in glucose homeostasis. Naturally occurring inactivating mutations in the GK gene have been linked to the maturity-onset diabetes of the young (MODY2), while activating mutations lead to hyperinsulinemia and/or hypoglycemia. Additionally, recently it has been shown that lactate is implicated in the antilipolytic actions of insulin, illustrating another link between carbohydrate and fat metabolism. We developed a mathematical model that exploits lactate kinetics observed during the FSGIT to estimate 1) liver GK activity, 2) hepatic lactate production, and 3) whole body lactate clearance. To test the working model of lactate, we used a set of 17 normal mongrel dogs in which FSGITs were conducted. Glucose and lactate data from the FSGITs were analyzed using the mathematical model to estimate the four parameters of the model. We were able to resolve all four parameters in 12 dogs. We conclude that this novel working model of lactate metabolism is well-formulated and capable of estimating GK activity and lactate turnover from lactate measurements obtainable from the FSGIT. Future goals include the estimation of the parameters of the model in canine model of obesity.

## 770-P

**Effect of Increasing Dietary Fat Intake on Markers of Skeletal Muscle Oxidative Capacity in Lean and Obese Adults**

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The inability to adapt to high fat diet may distinguish individuals who are prone to obesity. We compared the effect of increasing dietary fat intake under isocaloric conditions on the expression of genes involved in lipid and carbohydrate metabolism in lean (LN,  $N=11$ , BMI= $22.0 \pm 2.2$  kg/m $^2$ , age= $30 \pm 7$  yrs) and obese (OB,  $N=6$ , BMI= $35.1 \pm 4.1$  kg/m $^2$ , age= $38 \pm 7$  yrs)

adults. Biopsies were obtained from the vastus lateralis following consumption of a low fat diet (LF, 20% fat, 65% carbohydrate, 15% protein) and a high fat diet (HF, 50% fat, 35% carbohydrate, 15% protein). The LF and HF diets were consumed for 4 and 2 days, respectively. The HF diet increased the mRNA levels of AMPK $\alpha$ , PDK4, SIRT1, and CD36, but did not affect mRNA levels of PGC1 $\alpha$ , LPL, or COX-IV. Obesity was associated with high PDK4 and CD36 mRNA. HF diet-induced increases in PDK4 and CD36 mRNA was more profound in OB than LN. The HF diet had no effect on the total protein of AMPK $\alpha$ , SIRT1, or PGC1 $\alpha$ . However, the HF diet increased serine-172 phosphorylation of AMPK and decreased the amount of acetylated PGC1 $\alpha$  in both LN and OB. These data suggest an acute bout of isocaloric HF feeding led to significant adaptations in the skeletal muscle expression of genes involved in lipid and carbohydrate metabolism that would favor fat oxidation. While the response was generally similar for LN and OB, certain adaptations (PDK4 and CD36 mRNA) were more substantial with obesity.

## 771-P

**Lower Mitochondrial Proton Leak in Primary Myotubes From Obese Diet-Resistant Versus Obese Diet-Sensitive Patients**

Rui Zhang, Erin L. Seifert, Ruth McPherson, Robert Dent, Mary-Ellen Harper *Ottawa, Canada*

We previously characterized obese patients in the lower and upper quintiles for weight loss rate in highly compliant sub-populations in a clinical weight loss program (Harper *et al.* 2002; Gerrits *et al.* 2010). Sub-populations are referred to as obese diet-resistant (ODR) and diet-sensitive (ODS), respectively. Skeletal muscle is a major contributor to basal metabolic rate; mitochondrial H $^+$  leak therein can account for up to 50 % of resting tissue O $_2$  consumption. H $^+$  leak in *rectus femoris* mitochondria is lower in ODR than ODS patients (Harper *et al.*, 2002). Our aim was to determine if this is a cell autonomous phenomenon. Subsets of ODR and ODS ( $n = 6$ /group) completed the Ottawa Hospital Weight Management Program and consented to *vastus lateralis* biopsies after a period of weight stabilization (age:  $55 \pm 5$  for ODR,  $48 \pm 5$  for ODS; BMI:  $34 \pm 2$  for both ODR and ODS). Resting and maximal O $_2$  consumption rates of primary myotubes were similar between ODR and ODS, as was mitochondrial membrane potential. There were no obvious differences in mitochondrial content or distribution. Mitochondrial UCP3 protein content was similar. However, H $^+$  leak was significantly lower ( $P < 0.004$ ) in ODR vs. ODS myotubes, whether cells were differentiated in low (5mM) or high (25mM) glucose. Thus, decreased mitochondrial H $^+$  leak in ODR compared to ODS muscle is a cell autonomous phenomenon, *i.e.*, does not depend on the *in vivo* neurohumoral environment. Genetic or epigenetic factors may be involved.

**Metabolic Aspects**

## 772-P

**Effect of Altering the Dietary Carbohydrate to Protein Ratio on Body Composition and Glycemic Control in Type 2 Diabetes**

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Hypothesis: By making up deficient proteins in diet, up to standard recommended levels, that too at every meal, in the usual low protein diabetic diet, would improve body composition & glycemic control. Methodology: 17 Type 2 diabetics (7cases, 10 controls) of either sex, aged 18-60 yrs, with HbA1c 7.5-10, stable weight ( $\pm 3$  kgs in 3 months) & therapy were enrolled. Patients with diabetic nephropathy, secondary obesity, neuropsychiatric disorders or on weight altering drugs were excluded. Electronically measured, sealed protein supplements were provided at every meal, for 3 months, to achieve an ideal carbohydrate-protein ratio, through a structured diet chart containing calories determined by the BMR. Subject food/activity diary records were assessed for compliance. Anthropometry, body composition (using Inbody 230 Body Composition Analyzer), glycemic control, renal functions & lipid profile were assessed. Results: Baseline Body Mass Index (BMI), Waist Circumference (WC), Waist Hip Ratio (WHR), Body Fat Percentage (BFP), Glycemic control & lipid profile in both groups were similar. There was a statistically significant percentage reduction in the WC (cases  $10.6 \pm 5.8$ , controls  $3.1 \pm 2.1$ ;  $p$  value = 0.001) & the WHR [Cases  $8.2 \pm 5.4$ , Controls  $1.2 \pm 2.3$ ;  $p$  value = 0.002]. Significant

reduction in the percentage rise of post prandial sugars (cases  $23.9 \pm 20.71$ , controls  $71.8 \pm 40.56$ ) was seen. ( $p$  value = 0.002) There was no significant change seen in BMI, weight, lipids and renal parameters between the groups. Conclusion: Carbohydrate:Protein Ratio maintenance helps reduce the sharp prandial glucose rise [responsible for oxidative stress] & abdominal type of obesity (metabolically active) i.e. WC & WHR. Larger studies are required to confirm this hypothesis

**773-P**

**Awareness of Childhood Obesity as a Health Hazard Amongst a Sample of Parents Living in an Inner-City Area of Palermo, Italy**  
Antonino Bianco, Caterina Mammina *Palermo, Italy*; Antonio Paoli Padova, *Italy*; Marianna Bellafiore, Giuseppe Battaglia *Palermo, Italy*; Monèm Jemni *United Kingdom*; Antonio Palma *Palermo, Italy*

Prevalence of overweight and obesity is approximately 40% in Sicilian schoolchildren at age 11 and over 25% at age 15. The objective of this study was to evaluate knowledge, perception and awareness of the obesity as a condition amongst a sample of parents living inner-city areas of Palermo, Italy. A cross-sectional survey was performed enrolling 311 parents/graduates of children attending schools located in inner district of Palermo, Italy, with low to medium income. Association of answer patterns with socio-demographic characteristics was evaluated by univariate and multivariate regression analysis. Although 83% considered weight excess in children as a health hazard, 30% considered it as a healthy condition. Junk food/beverages (78.0%), fast food (63.2%) and lack of exercise in school curriculum (48.7%) were identified as the most significant contributors to childhood obesity. Responsibility in tackling childhood obesity varied significantly according to the education level of the parents: low educated mothers less frequently perceived junk food/beverages, lack of exercise at school, lack of places to exercise and lack of security as threats to children health. Furthermore, mother's low education was negatively associated with their awareness of the roles played by food companies, school and healthcare services in the childhood obesity causative network. An increasing public awareness is required as key variable role in order to tackle the childhood obesity crisis.

**774-P**

**Nail Selenium Concentration Is a Negative Predictor of Circulating Levels of Oxidized Low Density Lipoprotein**

Josefina Bressan, Kiriaque B.F. Barbosa, Ana Carolina P. Volp *Vicosa, Brazil*; Inigo Blasco-Navarro, Jose Alfredo Martinez *Pamplona, Spain*

Background: Oxidized LDL (oxLDL) is a reliable marker of cardiovascular disease that plays an important role in the pathogenesis of atherosclerosis process. Metabolic syndrome is associated with increased mortality from cardiovascular events. This study evaluated plasma oxLDL concentrations and their association with anthropometric, biochemical and dietary intake in healthy young adults. Methods: This study was carried out with 160 subjects aged between 18 and 35 years (92 women and 68 men; body mass index:  $22.0 \pm 2.9$  kg/m<sup>2</sup>). Anthropometric, blood pressure and dietary intake (72-h food record) data were collected following standardized protocols. Fasting blood samples were collected for the measurement of glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triacylglycerols, insulin, uric acid, ceruloplasmin and oxLDL concentrations. Selenium, copper and zinc concentrations were assessed in nail samples. Values of  $p < 0.05$  were considered statistically significant. Results: Body mass index, truncal fat, systolic blood pressure, total cholesterol, LDL-c, triacylglycerol, total cholesterol-to-HDL-c ratio, uric acid serum levels and cholesterol daily intake were statistically higher between subjects with higher plasma oxLDL concentrations ( $> 69.36$  U/L). Nail selenium and copper values were statistically lower. By linear regression analysis, serum total cholesterol, LDL-c, total cholesterol-to-HDL-c ratio, and uric acid were positive predictors of oxLDL levels. On the other hand, nail selenium concentration was a negative predictive factor of this oxidative biomarker. Conclusions: OxLDL were predicted by selenium status and several anthropometric, biochemical and dietary intake data related to the development of metabolic syndrome.

**775-P**

**Subclinical Atherosclerosis in Latino Youth: Progression of Carotid Intima Media Thickness (CIMT) and Its Relationship to Cardiometabolic Risk Factors**

Claudia M. Toledo-Corral, Jaimie N. Davis, Tanya L. Alderete, Marc J. Weigensberg, Christina Ayala, Yanjie Li, Howard Hodis, Michael I. Goran *Los Angeles, CA*

Objective: To assess CIMT change ( $\Delta$ CIMT) over 2 years in overweight Latino adolescents and examine its relationship to cardiometabolic risk. Methods: 72 healthy overweight male and female Latino adolescents (mean age:  $14.5 \pm 1.7$  yrs; mean BMI:  $31.5 \pm 6.9$  kg/m<sup>2</sup>) were evaluated at baseline and 2 years later for: CIMT by high resolution B-mode ultrasound, body composition by DEXA and MRI, and glucose/insulin measures by fasting blood, and oral and intravenous glucose tolerance tests. Results: CIMT at baseline did not differ from 2-year follow-up; however 38 participants increased CIMT (Mean progression:  $0.017 \pm 0.003$ mm; +2.8%) and 34 decreased (Mean regression:  $-0.019 \pm 0.002$ mm; -3.1%). ANCOVA analyses show that participants with CIMT progression had higher baseline LDL-cholesterol and total cholesterol ( $91.3 \pm 3.4$  and  $150.3 \pm 3.9$ mg/dL) compared to those with CIMT regression ( $78.1 \pm 3.6$  and  $135.6 \pm 4.2$ mg/dL,  $p < 0.05$ ), independent of gender, baseline CIMT, age, and height. Adiposity and other measures of insulin action had no significant relationships with  $\Delta$ CIMT. In multivariate regression, LDL-cholesterol was the sole predictor of CIMT progression, but the effect was small (odds of CIMT progression increased by 3% for each 1 mg/dL higher baseline LDL-cholesterol [95% confidence interval (CI), 1.004-1.006,  $p = 0.03$ ]. Conclusions: These results indicate a high variability in the magnitude of  $\Delta$ CIMT in growing overweight Latino youth. Adiposity and insulin resistance were not associated with  $\Delta$ CIMT and LDL-cholesterol was the sole predictor of CIMT progression. These results support the use of LDL-cholesterol to assess sub-clinical atherosclerosis risk in overweight Latino youth.

**776-P**

**Modest Weight Loss By a Soy Peptides Containing Low Calorie Diet Is Associated With Favorable Changes in Plasma Adipocytokines and Metabolic Parameters**

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Obesity is associated with increased risks of metabolic syndrome, type 2 diabetes, cancers and other diseases. The hormones and cytokines produced by the adipose tissue may play an important role in obesity-related complications. In this study, we investigated the effects of weight loss by consuming soy peptides containing low calorie diets on plasma adipocytokines, anthropometric and metabolic parameters. Soy peptides were obtained by hydrolyzing soy flakes with the enzymes collected from the fermentation liquid. Twenty four overweight subjects (BMI $>25$ ) were recruited to follow a low calorie dieting with 20 g soy peptides (1500 kcal/d) daily for 8 weeks. Anthropometric data were measured every week, and biochemical data before and after the 8-week experiment were compared. Results showed that body weight, body mass index, body fat percentage, and waist circumference were significantly decreased ( $P < 0.001$ ). Serum total cholesterol, low-density lipoprotein cholesterol, triglyceride and liver function parameters were also decreased ( $P < 0.05$ ). A significant reduction ( $P < 0.005$ ) on plasma insulin concentrations and improvement of insulin resistance were also observed. In addition, there were significant decreases in serum leptin, resistin and CRP levels, and a rise in serum adiponectin ( $P < 0.01$ ). These results revealed that the application of soy peptides on low calorie diet for weight management is not only associated with the improvements in insulin sensitivity and lipid profile, but also the potentially favorable changes in serum adipocytokines.

**777-P**

**Vitamin D Deficiency in Morbidly Obese Women and Men**

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Background: Obesity is associated with vitamin-D deficiency. Body composition, body fat percentage and regional fat distribution differ between genders. We aimed to explore possible gender-specific differences in vitamin-D status in a cohort of morbidly obese Europoid patients. Methods: Vitamin-D

intake was assessed using a validated food-frequency questionnaire. Radioimmunoassay-analysis was used to measure 25-hydroxyvitamin D [25(OH)D]. Vitamin-D deficiency was defined as serum 25(OH)D <50 nmol/L (<20 ng/ml). Statistics; Mann-Whitney test, independent samples t-test, chi-square test, and logistic regression. Results: A total of 153 consecutive morbidly obese patients (112 women) with a mean (SD) age of 43.5 (10.8) years and BMI 44.7 (6.3) kg/m<sup>2</sup> were included. The male and female groups were comparable with respect to age, BMI and season of blood sampling. Male patients had a larger waist circumference; 141 (13) versus 129 (13) cm,  $p < 0.001$ , and a numerically higher median vitamin-D intake than women; 9.7 versus 8.2  $\mu\text{g/day}$  ( $p = 0.073$ ), whilst significantly more men than women had vitamin-D deficiency; (73% versus 46%,  $p = 0.006$ ). Simple logistic regression showed that men had 3-fold increased odds of vitamin-D deficiency (OR=3.15, 95%CI 1.44-6.90,  $p = 0.004$ ). Multiple logistic regression revealed that male gender remained associated with vitamin-D deficiency (OR=2.62, 95%CI 1.05-6.53,  $p = 0.039$ ) after adjustment for waist circumference (OR=1.05, 95%CI 1.02-1.08,  $p = 0.001$ ), age (OR=0.96, 95%CI 0.93-1.00,  $p = 0.023$ ), vitamin-D intake (OR=0.96, 95%CI 0.90-1.02,  $p = 0.176$ ) and season of blood sampling (OR=0.78, 95%CI 0.39-1.58,  $p = 0.489$ ). Conclusion: Male gender is associated with vitamin-D deficiency in Norwegian morbidly obese patients. This might partly be explained by larger waist circumference.

### 778-P

#### Sleep Duration, Napping Duration, and Insomnia Are Related to Metabolic Risk Factors in Young Latina and African American (AA) Females

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Background: Sleep deprivation is associated with obesity and metabolic risk factors. However, relationships between sleep and obesity-related metabolic risk are understudied in minority children. Objective: To investigate the relationships between sleep and metabolic outcomes in Latina and AA females. Methods: Cross-sectional data from 36 participants is presented (69.4% Latina,  $M_{\text{age}} = 10.1 \pm 1.2$ ). Sleep duration, napping duration and insomnia were measured by questionnaire. Metabolic measures included lipids, blood pressure (BP), serum/salivary cortisol, insulin indices, and body composition by BodPod™. Relationships between sleep and metabolic risk factors were assessed using t-tests and partial correlations, adjusting for ethnicity, Tanner stage, and fat/lean mass where appropriate. Results: Sleep duration per night was correlated with systolic ( $r = -0.76$ ,  $p < 0.001$ ) and diastolic BP ( $r = -0.56$ ,  $p = 0.017$ ). Sleep duration on weekdays was correlated with triglyceride ( $r = -0.54$ ,  $p = 0.021$ ) and systolic ( $r = -0.73$ ,  $p = 0.001$ ) and diastolic BP ( $r = -0.52$ ,  $p = 0.027$ ). Napping duration on weekdays was correlated with disposition index ( $r = 0.42$ ,  $p = 0.025$ ) and salivary cortisol awakening response ( $r = -0.67$ ,  $p = 0.012$ ). Napping duration on weekends was correlated with triglycerides ( $r = 0.65$ ,  $p < 0.001$ ) and percent body fat ( $r = 0.50$ ,  $p = 0.033$ ). Those with insomnia had higher triglycerides ( $p = 0.024$ ) and serum cortisol ( $p = 0.034$ ) than those without. Conclusions: Nighttime sleep duration and napping duration on weekdays were associated with lower levels of metabolic risk factors. Insomnia and napping during weekends were related to adverse metabolic outcomes. Longer nap time on weekends may be compensating for sleep debt, which may be responsible for poor metabolic outcomes. Sleep habits appear to be important factors to consider when studying metabolic health in children.

### 779-P

#### Profound and Recalcitrant Vitamin D Deficiency in 208 Biliopancreatic Diversion Patients: A Retrospective Study

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Biliopancreatic Diversion (BPD) is a drastic and irreversible form of bariatric surgery that produces substantial and sustained weight loss, improved co-morbidities, and a higher quality of life. However, it does have associated sequelae such as vitamin D deficiency. With limited published data, a comprehensive review of vitamin D levels in BPD patients was warranted. Post-operative 25-hydroxyvitamin D (25-OH-D) levels were assessed from 208 BPD patients. All patients underwent the surgery at Creighton University Medical Center (CUMC) by one surgeon from 1999-2008. CUMC is in Omaha, NE which is located at latitude 41.3° N. Seasonal variations were not considered during the study. Daily oral supplementation of 50,000

I.U. vitamin D3 was prescribed to each patient following surgery. The data showed that the majority (73.1%) of BPD patients had insufficient ( $\leq 30$  ng/ml) levels of 25-OHD with 47.6% of BPD patients fitting the criteria of vitamin D deficiency ( $\leq 20$  ng/ml). Other gathered data included patient sex (81% female; 19% male), ethnicity (98% white; 2% African American), age (mean=45.6±9.6), and days after surgery (mean=954±661) that vitamin D levels were measured. This study gives evidence that profound and recalcitrant vitamin D deficiency is prevalent in BPD patients despite extreme levels of oral vitamin D supplementation. Low levels of vitamin D contribute to osteoporosis, cancer, lower immune status, and other unknown sequelae with potentially serious implications. In addition to increased long-term monitoring of vitamin D deficiency in BPD patients, new protocol of vitamin D supplementation may need to be developed.

### 780-P

#### How Do Manipulations in Fat Content of Laboratory Test-Meals Impact Children's Liking and Consumption of These Foods?

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Background: US children consume diets too high in palatable, energy dense foods, making them at risk for developing obesity. Increased knowledge of factors driving these food choices might improve the development of obesity interventions. Aim: The aim of this study was to investigate the effects of manipulating the fat content of test-meal foods on reported liking, intake, and body composition in children. Method: 56 children (20 boys/36 girls, mean age: 5.14±0.76 years, mean BMI z-score: 1.18±0.95) with diverse ethnic backgrounds participated in this cross-sectional study. Children attended four laboratory sessions, two of which are reported here, where liking and intake were assessed for a test-meal consisting of macaroni and cheese, pudding, chocolate milk and white milk. Children received the foods as either high-fat (34-48% calories from fat) or low-fat (0-11% calories from fat). Liking for each food was assessed by 5-pt facial hedonic scale and intake as pre- and post-weight difference. Anthropometrics (ht/wt) and body composition (DXA) were also measured. Results: Mean intake from the high and low-fat meals were highly correlated ( $r = 0.80$ ,  $p < 0.000$ ), as were mean reported liking ratings for the meals ( $r = 0.67$ ,  $p < 0.000$ ). In addition, children's total % body fat was positively correlated to mean intake of high-fat foods ( $r = 0.42$ ,  $p = 0.003$ ) and low-fat ( $r = 0.36$ ,  $p = 0.012$ ) foods, but not to mean reported liking of those foods. Conclusion: Results suggest that children's consumption and liking for laboratory manipulated high- and low-fat foods differs little. If replicated, parents might reduce fat content of well-liked foods as a means of improving children's diets.

### 781-P

#### The Impact of Television on Food Intake: The Role of Gender, Advertisements, and Transportability

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Obesity, a health problem of epidemic proportions, is associated with significant health and psychosocial consequences. Although television viewing itself may lead to decreased energy expenditure via engagement in sedentary behavior, exposure to food-related advertisements may be associated with increased caloric intake. Therefore, the purpose of the present study was to examine the impact of television commercials on food intake according to gender and transportability, or the tendency to become engrossed in what one is viewing. Undergraduate men ( $n = 40$ ) and women ( $n = 40$ ), free of disordered eating attitudes and behaviors, at a private Midwestern university were randomly assigned to one of three conditions (a sitcom with food-related advertisements, neutral advertisements, or no advertisements) for one hour. Participants completed measures of transportability and study stimuli. The number of cookies consumed during the experiment was recorded. Contrary to expectations, no significant main effects or interactions involving advertisement condition, gender, or levels of transportability were found after controlling for relevant variables. However a statistical trend was present for a main effect of transportability ( $F = 3.02$ ,  $p = .08$ ,  $\eta^2 = .06$ ), with participants who scored high on transportability ( $M = 5.52$ ,  $SD = .79$ ) eating more cookies than participants who scored low on transportability ( $M = 3.61$ ,  $SD = .75$ ). These results suggest that food intake was not affected by the advertisement condition or the participant's gender; however, their food intake may be influenced by their level of transportability. Future research is needed to examine the impact of individual difference variables on the relationship between food-related advertising and food intake.

**782-P****Insulin Resistance and Non Alcoholic Fatty Liver Disease in Hispanic Adolescents**

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Nonalcoholic fatty liver disease (NAFLD) is characterized by accumulation of fat in the hepatocytes. NAFLD disorders can range from simple steatosis to chronic end-stage liver disease. In children, NAFLD is the most common liver disease and is thought to be associated with insulin resistance. The purpose of this study was to determine the associations between insulin resistance and hepatic fat fraction (HFF) and liver enzymes (ALT, AST) as measures of NAFLD in Hispanic adolescents. Thirty-two Hispanic adolescents (BMI  $\geq$  95<sup>th</sup> percentile; 14 males, 18 females), mean ( $\pm$  SD) age 14.5 ( $\pm$ 1.6) years participated in the study. HFF was measured via magnetic resonance imaging. Fasting blood samples were collected for measurements of ALT, AST, insulin and glucose. Homeostasis model assessment (HOMA) and fasting insulin were used as measures of insulin resistance. Spearman correlation analyses were conducted to determine associations between variables. Mean ( $\pm$ SD) HFF, ALT, AST, fasting insulin, HOMA and fasting glucose were 3.1% ( $\pm$ 7.3), 18.8 U/L ( $\pm$ 7.7), 18.8 U/L ( $\pm$ 4.5), 9.1  $\mu$ IU/mL ( $\pm$ 4.3), 2.0 ( $\pm$ 1.0) and 88.6 mg/dl ( $\pm$ 6.2). There were no significant differences in HFF, ALT, AST, fasting insulin, and HOMA between boys and girls. HOMA was positively correlated with HFF ( $r=0.42$ ,  $p<0.05$ ) and ALT ( $r=0.35$ ;  $p<0.05$ ) but not AST. Fasting insulin was positively correlated with HFF ( $r=0.45$ ,  $p<0.01$ ) but not ALT or AST. Results showed significant associations between insulin resistance and surrogate markers of NAFLD in overweight Hispanic adolescents. Overweight Hispanic youth may be disproportionately affected by NAFLD because of the high prevalence of overweight and insulin resistance.

**783-P****Associations of Adipocytokines and Anthropometric Measurements of the Newborns of Pregnant Women With Abnormal Screening of 50g Glucose Tolerance Test in State of Qatar**

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Background: Adipose tissue secretes several adipocytokines that may play an important role in development of insulin resistance during pregnancy. The aim of this study is to investigate the associations of these adipocytokines with anthropometric measurements of the newborns of pregnant women with abnormal 50g glucose tolerance test [GTT] results. Methods: The study subjects included all pregnant women (n=85) of matched age and BMI, that showed abnormal results to 50g [GTT]. During 100g [GTT], fasting blood samples were analyzed for glucose, lipid profile, IL-6, TNF- $\alpha$ , Hs-CRP, insulin, and total adiponectin. Results: 100g [GTT] showed that 60% were normal [C] and 40% had impaired glucose tolerance [IGTT]. Of all biochemical measured, only glucose (fasting, 1h, 2h, and 3h) and insulin were significantly higher in [IGTT] group than [C] group. Mean values  $\pm$ SD: IL-6 (2.56 $\pm$ 1.16 vs. 2.49 $\pm$ 1.63 pg/ml,  $p=0.80$ ), TNF- $\alpha$  (3.86 $\pm$ 2.52 vs. 5.16 $\pm$ 3.45 pg/ml,  $p=0.07$ ), Hs-CRP (48.59 $\pm$ 17.03 vs. 50.18 $\pm$ 18.19 ng/ml,  $p=0.69$ ), and total adiponectin (15.97 $\pm$ 8.09 vs. 14.65 $\pm$ 7.15  $\mu$ g/ml,  $p=0.31$ ) among [C] and [IGTT], respectively. No significant differences were observed for anthropometric measurements studied such as birth weight (3209.66 $\pm$ 463.57 vs. 3558.50 $\pm$ 80.66 g,  $p=0.74$ ), placenta weight [PW], ponderal index [PI] and birth weight/placental weight index [FPI] between [C] and [IGTT] groups, respectively. TNF- $\alpha$  was positively correlated significantly with IL-6 ( $r=0.29$ ,  $P=0.012$ ), PW ( $r=0.48$ ,  $P=0.017$ ) and negatively with FPI ( $r=-0.47$ ,  $P=0.019$ ), gestational age "GA" ( $r=-0.41$ ,  $P=0.043$ ) and total adiponectin ( $r=-0.28$ ,  $P=0.016$ ). Conclusion: Marked hyperglycemia and hyperinsulinemia were observed in IGTT. Of all adipokines measured, TNF- $\alpha$  had a significant relationship with PW, FPI, and GA.

**784-P****Sex and Age-Dependent Increases in Circulating Leptin and Pro-Inflammatory Cytokines in Overweight Pre-School Aged Children**

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Overweight and obesity are significant public health concerns and are associated with a chronic state of inflammation, characterized by elevated levels of circulating pro-inflammatory cytokines in adolescents and adults. However, the effect of overweight/obesity in pre-school aged children with

no other associated co-morbidities is not well characterized. Fasting blood plasma was collected from 86 healthy weight (BMI percentile 5-84%) or overweight (BMI percentile greater than 85%) pre-school aged children aged 2-6 years old. Plasma leptin was quantified by a commercially available radioimmunoassay. Interleukin-1 b (IL-1 $\beta$ ), Interleukin-6 (IL-6), and Tumor Necrosis Factor alpha (TNF $\alpha$ ) were quantified by commercially available ELISA kits. Plasma leptin was significantly elevated in overweight (OW) subjects compared to healthy weight (HW) controls (3.0 vs. 6.3 ng/ml). Females exhibited significantly elevated serum leptin compared to males, irrespective of weight status (HW, 3.2 vs. 2.6 ng/ml; OW, 8.3 vs. 4.2 ng/ml). OW males exhibited elevated IL-1 $\beta$  compared to HW males (1.18 vs. 0.5 pg/ml). OW 2-4y subjects, but not OW 4-6y subjects exhibited significantly elevated levels of IL-1 $\beta$  (1.1 vs. 0.48 pg/ml) and TNF $\alpha$  (2.42 vs. 1.96 pg/ml). No differences in plasma IL-6 were found between OW and HW subjects. Compared with HW children, OW children as young as age 2 developed significantly elevated levels of plasma leptin, and age- and sex-dependent increases in circulating pro-inflammatory cytokine concentrations. Development of childhood overweight or obesity could contribute to a state of chronic inflammation at an early age in otherwise healthy pre-school aged children.

**785-P****DASH Score Predicts Vascular Function and Insulin Resistance Among Normotensive Lean and Obese African American Women**

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Proposed mechanisms of impaired nitroglycerine-mediated dilation (vascular function) observed in African Americans (AA) include genetic susceptibility or lifestyle factors. We examined cross-sectional associations between habitual adherence to a Dietary Approaches to Stop Hypertension (DASH)-type diet, and indices of vascular function and insulin resistance in healthy, normotensive, lean and obese AA women (age 18-45, n=52). Diets were assessed with Willet's AA-food frequency questionnaire; nitroglycerine-mediated dilation by high-frequency ultrasound; insulin resistance by the homeostasis model assessment (HOMA), adiponectin and high sensitivity C-reactive protein (hsCRP) by immunoassay; data is mean  $\pm$  s.d. Adherence to a DASH-type diet was poorer in study subjects relative to a reference population (women's Health Study) as evidenced by lower dietary intake of fruits (1.27  $\pm$  1.5 versus 2.19  $\pm$  1.4 servings/day), and higher intake of sodium (2,360  $\pm$  1,370 versus 2,070  $\pm$  760 mg/day) and sweetened beverages 2.33  $\pm$  2.2 versus 0.26  $\pm$  0.56 servings/day, all  $p < 0.01$ . Body mass index was an independent predictor of adiponectin, hsCRP and HOMA all  $p < 0.05$ . The lowest versus the highest quintile of the DASH score was associated with lower nitroglycerine-mediated dilation, independent of age ( $\beta=0.29 \pm 0.14$ ;  $p=0.05$ ) BMI ( $\beta=0.29 \pm 0.14$   $p=0.04$ ) and blood pressure ( $\beta=0.31 \pm 0.14$   $p=0.03$ ). Also, intakes of sodium and sweetened beverages were independently associated with HOMA ( $\beta=0.0002 \pm 0.00006$   $p=0.004$ ;  $\beta=0.10 \pm 0.14$   $p=0.02$ ), respectively. Low DASH adherence scores and key components dietary sodium and sweetened beverages predicted vascular dysfunction and insulin resistance, respectively, in a cohort of AA women.

**786-P****Inverse Association of Serum Vitamin C Concentration and Weight Status in School-Aged Children**

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Childhood overweight and obesity are significant public health concerns that may result in abnormal growth and development. Although numerous studies have characterized vitamin C intake and serum levels, and have demonstrated an inverse association with obesity in adults, few studies have examined this association between serum vitamin C concentration and weight status in a pediatric population. The purpose of this study was to determine if increased serum vitamin C concentration in children was inversely associated with weight status in school-aged children. This study was a cross-sectional, retrospective study of 1,133 healthy weight or obese children aged 6-11 years included in the National Health and Nutrition Examination Survey (NHANES) datasets from 2003-2004 and 2005-2006, for whom relevant medical, socioeconomic, anthropometric data and serum vitamin C data were complete. Subjects were divided into two groups

based on their serum vitamin C concentrations. Bivariate analysis was conducted to identify significant associations between vitamin C concentration and weight status. 868 subjects were healthy weight (77%) and 265 subjects were obese (23%). Subjects in the lower 50% group had serum vitamin C concentrations of 0.16-1.34 mg/dL, and those in the upper 50% had 1.35-3.43 mg/dL. The odds ratio for obesity in subjects in the upper 50% of serum vitamin C values relative to the lower 50% was 0.41 (95% confidence interval= 0.27,0.61). These results suggest that serum vitamin C concentrations are inversely related to weight status in school-aged children. Increased vitamin C consumption could reduce the risk of development of childhood obesity.

**787-P****Improved Insulin Sensitivity and Decreased Insulin Secretion in Adolescents Undergoing Gastric Bypass**

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Insulin resistance (IR) is a key feature of most obesity-related comorbidities. Roux en Y gastric bypass (RYGB) causes substantial weight loss, but effects on IR and carbohydrate metabolism in adolescents are not fully understood. Intravenous glucose tolerance tests (IVGTT) were used to characterize metabolic responses to RYGB in adolescents before and 1 year after surgery. Twenty-three subjects studied included 2 with T2DM; age range 14-20 (mean 17 years); gender distribution 15F/8M; 18 Caucasian, 5 AA. Concomitant with mean ( $\pm$ SD) decrease in BMI from 60 $\pm$ 12 to 38 $\pm$ 8kg/m<sup>2</sup>, mean ( $\pm$ SD) insulin sensitivity (S<sub>i</sub>) increased 5-fold (0.79 $\pm$ 1 to 4.2 $\pm$ 3min<sup>-1</sup> pM<sup>-1</sup> [p<0.01]). While the acute insulin response to glucose, AIR<sub>g</sub>, decreased 2-fold (864 $\pm$ 482 to 380 $\pm$ 177 pmol/L [p<0.01]), when corrected for the changes in insulin sensitivity (disposition index) there was an increase of beta-cell function, although this did not reach statistical significance (772 $\pm$ 823 [baseline] and 1398 $\pm$ 1020 [1yr; p=0.26]). These data suggest that RYGB in adolescents significantly improves insulin sensitivity, associated with a compensatory decrease in insulin secretion after IV glucose stimulus. Further research is needed to determine the degree to which weight loss and improvement in carbohydrate metabolism will impact long term risks of diabetes and cardiovascular sequelae of persistent obesity in adolescents undergoing weight loss surgery.

**788-P****Differential Effects of High-Sugar (HS) and High-Fiber (HF) Meals on Glucose and Insulin Levels in Overweight Latino and African American (AA) Adolescents in an Acute Feeding Study**

Ernest Shen, Ting Liu, Marc J. Weigensberg *Los Angeles, CA*; Britni Belcher, Alicia R. Thornton, Laura J. Berman, Donna Spruijt-Metz *Alhambra, CA*

Background: Prolonged consumption of HS meals has been associated with a variety of negative health outcomes. Objective: To examine the differential acute effects of HS versus HF meals on glucose and insulin levels in overweight minority youth. Methods: Using a randomized cross-over design, participants took part in two 8-hour in-lab feeding visits during which they received either a HS or a HF breakfast and lunch, at least two weeks apart. Fasting plasma glucose (mg/dL) and insulin (mg/dL) were obtained pre-breakfast, and then every half hour post-breakfast for the first five hours of each visit. Area Under the Curve (AUC) and Incremental AUC (IAUC), adjusting for fasting levels, were computed for glucose and insulin. Paired t-tests were used to compare AUC and IAUC, between the two meal types. Results: Participants were 34 Latino and AA adolescents {Mean<sub>AGE</sub>=15.7( $\pm$ 1.04), 68% Male, 88% Latino}. Fasting glucose and insulin levels did not differ by meal type. IAUC and AUC were higher in the HS condition for both insulin (p=0.04, p=0.03, respectively) and glucose (p=0.01, p=0.01). Compared to the HF condition, postprandial levels of glucose and insulin were higher 30 minutes post-breakfast (glucose<sub>HS</sub> - glucose<sub>HF</sub>=16.1, p=0.001; insulin<sub>HS</sub> - insulin<sub>HF</sub>=98.1, p<0.001), and 30 minutes post-lunch (glucose<sub>HS</sub> - glucose<sub>HF</sub>=18.0, p=0.001; insulin<sub>HS</sub> - insulin<sub>HF</sub>=61.9, p=0.001), than in the HS condition. Conclusions: Consumption of HS meals resulted in higher acute and sustained levels of glucose and insulin than the HF meal. This may lead to prolonged insulin exposure, which could contribute to negative health outcomes.

**789-P****Role of TIP47 in Skeletal Muscle Lipid Metabolism During Endurance Exercise**

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Intramyocellular lipid (IMCL) is an important energy source during endurance exercise. TIP47 is one of the PAT family protein that plays an important role in the regulation of lipid storage and mobilization in adipocytes by regulating access of lipases to lipid droplets. However, the role of TIP47 in skeletal muscle is less clear, especially during exercise. We first showed that a pharmacological cocktail that increases both oxidative capacity and insulin sensitivity in human primary myotubes also decreases the expression of TIP47. Therefore, the purpose of this study was to identify TIP47 protein in resting human skeletal muscle and determine the acute effect of a prolonged moderate intensity exercise on TIP47. Twenty healthy men (age 24 $\pm$ 5y; BMI 23.5 $\pm$ 1.7kg/m<sup>2</sup>) were placed on a 2-day isoenergetic high-fat diet (70% fat, 15% protein). After an overnight fast, a *vastus lateralis* muscle biopsy was obtained before a moderate intensity (50% VO<sub>2max</sub>) exercise for ~1.5-2 hrs (to 650 kcal) on a stationary bicycle. Another muscle biopsy was taken immediately after the end of exercise. TIP47 was identified by immunohistochemistry and quantified by western blotting. IMCL content was measured by immunohistochemistry. One bout of moderate exercise did not change the IMCL content (25.3 $\pm$ 26.1 to 21.6 $\pm$ 19.8AU; p=0.4). There was however a ~21% trend for TIP47 to decrease from 0.19 $\pm$ 0.1 to 0.15 $\pm$ 0.08AU (p=0.06) after the exercise bout. This decrease in skeletal muscle TIP47 protein content in response to prolonged exercise suggests that TIP47 may play a role in lipid metabolism allowing enhanced lipolysis and lipid oxidation.

**790-P****Can Response to Six Weeks of Optifast 900 Meal Replacement in the Ottawa Hospital Weight Management Program (OHWM) Predict Weight Loss After Lap Roux-en-Y Gastroplasty?**

Robert Dent *Ottawa, Canada*; Matthew Fitzer *New Hartford, NY*; Gosh Sujoy *Durham, NC*; William Graber *New Hartford, NY*; Mary-Ellen Harper, Ruth McPherson *Ottawa, Canada*

We have previously characterized diet resistant and diet sensitive sub-populations of highly compliant patients on 6 wks of Optifast® (diet) (Harper *et al.*, 2002; Gerrits *et al.*, 2010). We then asked whether this response to diet predicted subsequent response to a Roux en Y gastroplasty. Of the 3264 patients who had completed the OHWM Sep. 1992 – Dec. 2008, 81 went on to have identical RY surgery by one of two surgeons at Faxon St. Luke's Medical Center. Of the 81 patients, 26 were excluded *a priori* because of poor program adherence or medical factors arising between treatments that would affect outcome, leaving 46 evaluable women and 9 men. We then determined correlations between % weight loss (from day 1) until 6 wks on diet and % weight loss from day 1 until 12 mos. after Roux-en-Y gastroplasty. Comparisons of weight loss: Women diet mean, (range): 10.2% (7.18% - 15.47%) vs surgery 35.7% (19.6% to 53.73%). Men: 11.6% (7.98% - 15.1%) vs 35.5% (27.8% to 42.5%). Bivariate fit of % weight loss surgery by % weight lost by diet revealed an R<sup>2</sup> value of 0.19 with a p-value of 0.0027. These findings demonstrate that diet response predicts subsequent response to surgery and these data may be of value in choosing the appropriate surgical procedure for individual patients. Further study is needed to determine if the patients with poor surgical outcomes also are characterized by unique gene expression and muscle metabolic phenotypes consistent with our previous studies of diet resistant versus diet sensitive patients.

**791-P****Continuous Glucose Monitoring to Assess the Ecological Validity of Glycemic Index in Obese Adults With Type 2 Diabetes**

Anthony N. Fabricatore *Philadelphia, PA*; Cara B. Ebbeling *Boston, MA*; Thomas A. Wadden *Philadelphia, PA*; David S. Ludwig *Boston, MA*

Dietary glycemic index (GI) refers to the rate at which carbohydrate is converted to blood glucose. It is derived empirically by comparing the glycemic responses to equivalent carbohydrate portions of a test food and glucose solution. A primary criticism of this construct is that the requirements of GI testing (consuming single items, at prescribed portions and rates, after an extended fast) do not reflect real-world eating conditions.

We used continuous glucose monitoring (CGM) to track participants' glycemic response to self-selected foods, consumed without artificial constraints. Participants were 29 adults with type 2 diabetes (79% women, mean  $\pm$  standard deviation age =  $50 \pm 9$  years, body mass index =  $36 \pm 5$  kg/m<sup>2</sup>) who were enrolled in a larger trial of lifestyle modification for weight loss. Dietary intake and blood glucose were tracked over two 3-day periods (at baseline and after 20 weeks of treatment). We analyzed food records to obtain GI and other dietary variables. These were examined in relation to several glycemic response variables, assessed by CGM. Mean daily GI was significantly related to mean 24-hour area under the curve ( $r = .54$ ), % of time in the euglycemic (71-180 mg/dl) and hyperglycemic (>180 mg/dl) ranges ( $r = .58$  and  $r = .57$ , respectively), and mean amplitude of glycemic excursions ( $r = .40$ ). No other dietary variable (kcal, % of kcal from fat/CHO/protein, total/added sugar, glycemic load) was significantly related to any glycemic response indicator. These results support the validity of the GI construct outside of the laboratory.

### 792-P

#### Fasting Insulin and Gamma Glutamyl Transferase (GGT) Predict Nonalcoholic Steatohepatitis (NASH) in Hispanic Children

Stephanie H. Abrams, E. O'Brian Smith, C. Wayne Smith *Houston, TX*

Background: Nonalcoholic steatohepatitis (NASH) affects 3% of all children and is most prevalent in Hispanic children. Currently, the only method of diagnosis is a liver biopsy which is both costly and invasive. Methods: To test the hypothesis that biomarkers exist for Hispanic children with NASH, 3 study groups were recruited: (1) obese children with a liver-biopsy demonstrating NASH in the 60 days prior to study visit, (2) obese children with no liver disease, and (3) lean children with no liver disease. Each child had blood drawn and serology was performed for lipid panel, hepatic panel, insulin, glucose, and uric acid. ELISA was performed for high-sensitivity c-reactive protein (hs-CRP), caspase generated cytokeratin-18 fragments (CK-18), fetuin-A, and adiponectin. Area under the curve ROC analysis was performed to differentiate Hispanic children with NASH from those without NASH. Results: 57 Hispanic subjects were recruited with a mean age of  $12.1 \pm 2.1$  years. The mean BMI z-score and BMI percentile for age/sex were the same for the NASH and obese control groups. Adiponectin was significantly lower, while Fetuin-A, HOMA-IR, and CK-18 levels were significantly higher in NASH subjects when compared with obese and lean controls. ROC analysis for fasting insulin + GGT demonstrated that a cut-off of 40.5 U/L+mg/dl predicted NASH vs. not-NASH with an AUC of 93.4%. Conclusion: Cytokeratin-18 fragments are significantly higher in obese Hispanic children with NASH compared to obese and lean controls. Fasting insulin + GGT may be an effective clinical tool for the pediatrician when managing the obese Hispanic child with elevated aminotransferases.

### 793-P

#### Weight Loss Response to Meal Replacement of One Sister in a Behavioral Program Correlates With the Weight Loss Response of the Second

Robert Dent *Ottawa, Canada*; Sujoy Ghosh *Durham, NC*; Mary-Ellen Harper, Ruth McPherson *Ottawa, Canada*

We have previously characterized diet resistant and diet sensitive sub-populations in highly compliant patients in response to 6 wks of Optifast® (diet) in the Ottawa Hospital multidisciplinary Weight Management Clinic program (Harper et al, 2002). To further explore the genetic basis of weight loss success, we compared rate of weight loss in female sibpairs with that of weight-, height-, age- and gender- matched controls. Methods: From a database of 2887 patients who had completed the OHWMC program Sep. 1992 – May 2007, we identified 27 sister pairs. A priori, 13 sister pairs were excluded due to, non adherence (8), or mobility restrictions likely to affect weight loss (5). We selected 4 unrelated, healthy and highly compliant female controls for each sib pair. They were matched to be within 1.5 cm in height, 3 Kg of initial weight and 8 years of age. Results: Our findings indicate that the percent weight losses were more closely matched for the sib pairs than for unrelated subjects. The absolute differences in the percent weight lost between sib pairs were overall smaller compared to the differences in percent weight lost for unrelated pairs. Tests of both variance (Brown-Forsythe  $p=0.03$ ) and group means (Welch ANOVA  $p=0.008$ ) demonstrated significant differences between the groups. Rank of sums of

absolute percent weight lost differences were also significantly different between the groups (Wilcoxon  $p=0.007$ ) Conclusion: This provides further evidence for a genetic basis for variability in weight loss success in response to a precise dietary regimen.

### Metabolic Correlates and Consequences

#### 794-P

#### Blood Gene Expression Profiling Prior to Caloric Restriction Demonstrates Upregulation of Oxidative Phosphorylation in Obese, Diet-Sensitive Subjects

Sujoy Ghosh *Durham, NC*; Robert Dent, Mary-Ellen Harper *Ottawa, Canada*; Joan Stuart *Research Triangle Park, NC*; Ruth McPherson *Ottawa, Canada*

Clinically, obesity represents a constellation of phenotypes associated with weight gain and weight loss, weight maintenance, and weight re-gain. Amongst compliant subjects enrolled in a structured weight loss program at the Ottawa Weight Management Clinic, we observed a 4-fold variation in the rate of weight loss in response to a 900 kcal diet after correction for initial body weight, gender and age. Subjects in the top and bottom quintiles of weight-loss success were considered to be obese, diet-sensitive (ODS) and obese, diet-resistant (ODR) respectively. Consistent with a hypothesis of altered energy metabolism, we have previously observed an increase in mitochondrial proton leak and upregulation of oxidative phosphorylation genes in skeletal muscle from ODS subjects as compared to the ODR subjects. We now extend these findings through whole-genome expression profiling of whole blood from ODS and ODR subjects, prior to the initiation of caloric restriction. Pathway enrichment analysis of gene expression profiles via multiple analytic tools converged on the "oxidative phosphorylation" pathway as being statistically significantly upregulated in obese, diet-sensitive subjects compared to the diet-resistant subjects. This is indicative of an enhanced capacity for mitochondrial energy harvest in obese subjects that may help partly explain the accelerated weight-loss in response to caloric restriction. The current study further highlights the utility of blood as a sentinel tissue reflecting systemic states and suggests the possibility for the identification of blood-based early predictors of weight-loss success.

#### 795-P

#### Serum Ferritin Was Interlocked With Aortic Stiffness in Obese Hypertensive Diabetic Koreans

Kyu Rae Lee, Won Yong Kim *Seoul, Korea*; Kyung Kon Kim, In Cheol Hwang, Kyung Sik Lee *Incheon, Korea*

To evaluate aortic stiffness through ba PWV (brachial ankle Pulse Wave Velocity) was observed as a useful screening tool for cardiovascular disease. Recent studies showed there was a positive association between serum ferritin and increased risk of myocardial infarction in smokers. Additionally owing to increasing prevalence of obesity, there was an increasing prevalence of cardiovascular disease. Thus we would like to compare serum ferritin and PWV in the subjects with hypertension and diabetes according to obesity. A total of 196 subjects (43.97 years, 25.5% women, BMI 23.92 Kg/m<sup>2</sup>), with diabetes and hypertension were investigated among those who underwent the periodic health examination at Hong Ik general hospital. The cut-off point of obesity in Korea had been defined as 25 kg/m<sup>2</sup>. Student's t-test was applied in order to compare the ferritin, ba PWV between two groups according to obesity using SPSS version 13.  $P < 0.05$  at both sided was considered as statistically significant. The means of serum ferritin ( $P=0.007$ ) and ba PWV ( $P=0.026$ ) in obese group were significantly higher than those in non-obese group. ( $P < 0.05$ ) In conclusion, serum ferritin might be regarded as an independent monitoring factor to atherosclerosis in obese hypertensive diabetic Koreans. Prospective well-controlled cohort study would be considered in the future.

#### 796-P

#### Insulin Resistance and Carotid Artery Intima-Media Thickness in Non-Diabetic Women

Lora Light, Larry Tucker *Provo, UT*

Background: This investigation was conducted to study the association between insulin resistance and its components, and common carotid artery (CCA) intima-media thickness (IMT), in 198 women using a cross-sectional design. Methods: Insulin resistance was indexed using HOMA (fasting insulin

( $\mu\text{U/mL}$ ) $\times$ fasting glucose (mg/dL)/405). IMT was measured using the SonoSite 180+, a B-mode, high-resolution, ultrasonograph equipped with a 5-MHz transducer. For each subject, 30 images were captured over a 1 cm segment, measured to the nearest 1/1000 mm, 1 cm proximal to the CCA bulb using SonoCalc software. Nine clear images were randomly selected and averaged to index IMT. Age, body fat percentage (BF%), measured using the Bod Pod, and physical activity (PA), assessed using Actigraph accelerometers for 7 consecutive days, were treated as potential confounders. Results: (Mean $\pm$ SD) age: 43.1 $\pm$ 3.0 years, glucose: 86.4 $\pm$ 6.3 mg/dL; insulin: 6.9 $\pm$ 3.0  $\mu\text{U/mL}$ ; HOMA: 1.5 $\pm$ 0.7; IMT: 0.57 $\pm$ 0.06 mm; BF%: 32.0 $\pm$ 7.9; PA: 2,671,423 $\pm$ 945,682 counts. Regression showed that HOMA (F=0.2, p=0.6456) and insulin (F=0.7, p=0.4114) were not associated with IMT. However, fasting glucose was related linearly to IMT (F=4.7, p=0.0306). When subjects were divided into two glucose groups split at the median (86 mg/dL), women with glucose levels above the median had IMT values (0.579 $\pm$ 0.065) significantly greater (F=5.5, p=0.0204) than those with glucose levels below the median (0.559 $\pm$ 0.054). Controlling for differences in age, BF%, and PA had little impact on the relationship. Conclusions: As normal fasting blood glucose levels increase, IMT levels tend to increase. Women with glucose levels above the median have significantly thicker carotid arteries than their counterparts.

**797-P****Fat Free Mass, Body Weight, and Bone Mineral Density of the Hip in Middle-Age Women: The Roles of Diet, Physical Activity, and Menopause**Elizabeth Fosson, Larry Tucker *Provo, UT*

Background: Women with less fat free mass (FFM) and/or lower body weight tend to have lower bone mineral density (BMD). The extent to which diet, physical activity (PA), and menopause influence these relationships is unknown. Methods: BMD of the hip was measured in 263 middle-age women using the Hologic 4500W DXA system. Total PA and intensity of PA were measured objectively using an Actigraph accelerometer worn for 7 consecutive days. Dietary calcium and vitamin D from food and beverages, as well as from supplements, were measured separately using the Block food frequency questionnaire. Results: Hip BMD was strongly related to fat free mass (FFM) ( $r=0.53$ ,  $p<0.0001$ ) and total body mass ( $r=0.40$ ,  $p<0.0001$ ), but less to fat mass ( $r=0.20$ ,  $p=0.0012$ ). For each 10 kg decrease in FFM, hip BMD decreased by more than one standard deviation ( $\beta=0.116$ ,  $F=101.4$ ,  $p<0.0001$ ). Mean hip BMD was: 0.934 $\pm$ 0.112. Controlling statistically for use of bone building drugs weakened the association between FFM and hip BMD by 15%, however, adjusting for differences in age, height, menopause status, calcium and vitamin D intake from food and beverages, and from supplements, body fat percentage, and objectively measured total, moderate, and vigorous PA, each had very little influence on the FFM and hip BMD relationship. Conclusions: The relationship between FFM and BMD of the hip in middle-age women is strong and robust. The association is not influenced by differences in age, height, menopause, calcium and vitamin D intake, body fat, or PA levels, including PA intensity.

**798-P****The Relationship Between Waist Circumference and Metabolic Syndrome in Newly Developed Type 2 Diabetes Mellitus Based on the Diabetes Case Management Program 2001, Taiwan**Martin M-T Fuh, Peggy P-C Chen, Chia-Ing Li *Taichung, Taiwan*; Hsiu Yueh Su *Taipei, Taiwan*; Chwen Tzuei Chang, Rong Hsing Chen, Ching Chu Chen, Cheng-Chieh Lin *Taichung, Taiwan*

Background and Aim: To evaluate the relationship between waist circumference and MetS and its effect on the onset of T2DM following by the development of primary prevention program. Materials and Methods: From Jan. 2006 to Jun. 2009, 865 newly developed T2DM, age over 40, were enrolled in DCMP 2001. The MetS defined was based on the ATP III-criteria. Patients were classified under 6 groups, MetS with waist component, waist required and non-waist required; MetS without waist component, with 2 other components and with more than 2 components; Non-MetS with waist component; Non-MetS without waist component, with other one component and without any component. Results: The case and percentage distributions of all of MetS and Non-MetS in both sexes and at different age stratified ranges were shown in Table 1. As a whole, there were 61.6% in female and 54.7% in male demonstrated in the MetS group, whereas 45.9% in female and 66.2% in male were showed in the groups without waist component.

The percentage distributions of onset of T2DM at different age stratified ranges from 40 to over 80 in these 6 groups were statistically significant difference ( $p<0.001$ ), however there was no linear relationship found by trend test in either MetS or Non-MetS group. Conclusion: The newly developed T2DM would be prone to occur in the groups of MetS as a whole rather than groups with waist component. A variety of clustering of components of MetS was not the risk factor in the age of onset of T2DM.

**799-P****Relationships Between Visceral Adipose Tissue Measurement Site and the Metabolic Syndrome in the Korean Population**Se-Hong Kim, Ju Hye Chung, Sang Wook Song *Seoul, South Korea*

Objective: Visceral adipose tissue (VAT) is presumed to play an important role in the development of metabolic syndrome (MS). The purpose of this study was to evaluate the influence of measurement location of VAT on the cardiometabolic risk factors and the MS in the Korean population. Methods: To assess abdominal fat distribution, five single-slice computed tomography (CT) images were obtained in 470 healthy subjects. The five CT images were obtained at the intervertebral space from L1 to S1 using known anatomical landmarks. Multiple logistic regression analysis was performed to assess the relationship between regional adipose tissue areas and MS. Results: All risk factors were more closely correlated with VAT than subcutaneous adipose tissue (SAT), except waist circumference and blood pressure. Images located at L2–L3 or L3–4 provided high correlations between VAT area and all cardiometabolic risk factors. The highest adjusted odds (per SD) between VAT and MS were the L2–L3 image in men (OR 4.53) and the L1–L2 in women (OR 4.87), which was higher than measures at L4–L5 (OR: 3.22 in men, OR: 4.71 in women). However, differences in OR between L1–L2 VAT (OR 4.87) and L4–L5 (OR 4.71) were not great in women. Conclusions: The results of this study suggest that abdominal adiposity based on a single-slice CT scan is highly site specific, and an image located in the upper abdominal level (L2–L3 in men, L1–L2 in women) were more strongly and consistently correlated with MS in the Korean population.

**800-P****Subcutaneous Abdominal Adipose Tissue (SAAT) and Hepatic Fat Fraction (HFF) Explain Higher Insulin-Like Growth Factor (IGF)-I and IGF Binding Protein-I Levels in Obese African Americans (AA) Compared to Obese Latino Teenagers**Tanya L. Alderete *Los Angeles, CA*; Courtney E. Byrd-Williams *Austin, TX*; Claudia M. Toledo-Corral, David V. Conti, Marc J. Weigensberg, Michael I. Goran *Los Angeles, CA*

Background: African American ethnicity and obesity are associated with higher IGF-I and higher IGF-I is a risk factor for cancer. It is unknown whether ethnic differences in body fat distribution can explain ethnic differences in IGF-I. Objective: To examine the interrelationships between IGF-I, IGFBP-I, and adiposity in obese AA and Latinos. Methods: 126 obese adolescents (49 AA, 77 Latinos) were assessed for: insulin sensitivity (SI) by IVGTT; total fat mass (TFM) and lean mass by DEXA and SAAT, visceral adipose tissue (VAT), and HFF by MRI. Multivariate regression models were used to explore the relationship between adiposity variables and IGF-I, IGFBP-I, and IGFBP-3 (ng/ml). Covariates included age, gender, Tanner, TFM, TLM, SI, and ethnicity. Results: IGF-I levels were 23.1% higher in AA compared to Latinos ( $p<0.05$ ). In AA and Latinos, IGF-I and IGFBP-I were inversely correlated with BMI, TFM, and VAT ( $r=-0.20$  to  $-0.33$ ,  $p<0.05$ ) while IGF-I was inversely correlated with HFF ( $r=-0.33$ ,  $p<0.01$ ) and IGFBP-I with SAAT ( $r=-0.22$ ,  $p<0.05$ ). There were no significant relationships with IGFBP-3. The relationship between IGF-I and SAAT and IGFBP-I and HFF differed by ethnicity. There was a significant interaction between SAAT\*Ethnicity ( $p<0.05$ ) and HFF\*Ethnicity ( $p<0.01$ ). AA with more SAAT had higher levels of IGF-I and AA with a lower HFF had higher IGFBP-I levels compared to Latinos. Conclusion: There are strong inverse relationships between IGF-I and IGFBP-I with measures of adiposity in AA and Latinos. The relationship between IGF-I and SAAT, and IGFBP-I and HFF differed by ethnicity, contributing to higher IGF-I levels in AA.

**801-P***This abstract has been withdrawn.*

**802-P****Circulating Oxidized LDL and Inflammation in Extreme Pediatric Obesity**

Anne L. Norris, Julia Steinberger, Andrea M. Metzger, Sarah Jane Schwarzenberg, Lyn M. Steffen, Aaron S. Kelly *Minneapolis, MN*

Background: Oxidative stress and inflammation are mechanisms involved in the development of atherosclerosis and type 2 diabetes mellitus but have not been well characterized in extreme pediatric obesity. The purpose of this study was to compare levels of oxidative stress (circulating oxidized LDL) and inflammation (C-reactive protein [CRP] and interleukin-6 [IL-6]) in extremely obese (EO) children to normal weight (NW) and overweight/obese (OW/OB) children. Methods: Oxidized LDL, CRP, IL-6, body mass index (BMI), blood pressure, and fasting glucose, insulin, and lipids were obtained in 225 children and adolescents (age 13.5±2.5 years; boys N=124). Participants were classified into three groups based on gender- and age-specific BMI percentile: NW (<85<sup>th</sup>, N=128), OW/OB (85<sup>th</sup>-98<sup>th</sup>, N=63) and EO (≥1.2 times the 95<sup>th</sup>, N=34). Measures were compared across groups using ANCOVA, adjusted for gender, age, and race. Tukey post-tests were used for group comparisons of oxidized LDL, CRP, and IL-6. Results: Blood pressure, insulin, and lipids worsened across BMI groups (all p<0.0001). Oxidized LDL (NW: 40.7±9.0 U/L, OW/OB: 45.9±12.0 U/L, EO: 63.5±13.8 U/L) and CRP (NW: 0.5±1.0 mg/L, OW/OB: 1.4±2.9 mg/L, EO: 5.6±4.9 mg/L) increased significantly among BMI groups (all groups differed with p<0.01). IL-6 was significantly higher in EO (2.0±0.9 pg/mL) compared to OW/OB (1.3±1.2 pg/mL, p<0.001) and NW (1.1±1.0 pg/mL, p<0.0001) but was not different between NW and OW/OB. Conclusions: Extreme pediatric obesity, compared to milder forms of adiposity and normal weight, is associated with higher levels of oxidative stress and inflammation, suggesting elevated risk for premature cardiovascular disease and type 2 diabetes.

**803-P****Comparison of Metabolic Parameters in Patients With Bardet-Biedl Syndrome and BMI-Z Matched Controls**

Joan C. Han, Penelope P. Feuillan, David Ng, Julie C. Sapp, Yuqian C. Zheng, Jack A. Yanovski, Leslie G. Biesecker *Bethesda, MD*

Background: Bardet-Biedl syndrome (BBS) is a genetically heterogeneous disorder within a group of ciliopathies associated with obesity. In BBS mouse models, leptin signaling is impaired, and hyperleptinemia precedes onset of obesity. Methods: 50 patients with BBS were matched 2:1 with 100 healthy controls by age (BBS vs. control: 14.8±11.1 vs. 15.3±11.0y, p=0.68), sex (50%F each group), race (98% Caucasian each group), BMI (31.7±9.7 vs. 31.5±8.4kg/m<sup>2</sup>, p=0.96), and BMI-Z (2.17±0.89 vs. 2.10±0.84, p=0.60). Groups were compared for differences in body composition (DEXA, abdominal MRI), blood pressure (BP-Z, standardized for age, sex, height), fasting serum leptin, lipids, insulin, and glucose. Results: Patients with BBS had body fat% similar to control (42.1±8.5 vs. 39.4±10.5%, p=0.19), but higher visceral adiposity (%total fat at L2/3+L4/5: 26.9±10.4 vs. 19.7±6.1, p=0.001), higher DBP-Z (0.72±0.80 vs. 0.14±0.73, p<0.001), higher leptin (42.1±28.5 vs. 23.7±16.3ng/mL, p<0.001), and higher triglycerides (182±133 vs. 112±88 mg/dL, p<0.001). In subgroup analyses of most common genotypes, patients with *BBS1* mutations were similar to controls for all variables, whereas the differences in visceral fat, DBP-Z, leptin, and triglycerides between patients with *BBS10* mutations and controls persisted. Conclusions: Patients with BBS have higher leptin than expected for their degree of adiposity, consistent with leptin signaling dysfunction. Preferential deposition of fat intra-abdominally may predispose to metabolic complications. Patients with *BBS1* vs. *BBS10* mutations display different metabolic phenotypes. These results suggest that the obesity of BBS is distinct from nonsyndromic obesity and that there is heterogeneity in both genotype and clinical phenotype among the causative BBS loci.

**804-P****Cluster Analysis Reveals Important Determinants of Cardiometabolic Risk Patterns in Filipino Women**

Niha Zubair *Carrboro, NC*; Linda S. Adair *Chapel Hill, NC*

Background: With modernization, The Philippines has experienced increases in adiposity and associated cardiometabolic (CM) disease risk. Studying patterns of co-occurrence of risk factors may offer insights into etiology of CM diseases. Methods: Participants include 1,778 women assessed in the 2005 Cebu Longitudinal Health and Nutrition Survey. We

used cluster analysis to identify groups of women (age 48.3±6yr) sharing similar CM characteristics. Variables used to create the clusters included Z-scores of fasting triglycerides (TAGs), HDL-C, LDL-C, C-reactive protein (CRP), systolic and diastolic blood pressure (BP), HOMA-IR, and fasting glucose. We identified predictors of group membership using multinomial logistic regression. Results: We identified 4 distinct clusters which reflect: (1) low levels of all risk factors - "healthy", (2) low HDL-C in the absence of other risk factors, (3) elevated BP, and (4) insulin resistance (IR), elevated TAGs, and high fasting glucose. Groups were differentiated by age, menopausal status, SES, saturated fat intake, overweight status (OW=BMI>23), and most strongly by high waist circumference (WC>80). Women with high WC were much more likely to be in the IR (OR 4.76, 95% CI=2.38;9.51) or elevated BP group (2.99, 95% CI=2.06;4.34) compared to healthy women. After accounting for high WC, OW status did not predict membership in the low HDL-C or IR groups. Likelihood of being in the low HDL-C group, was increased uniquely by being premenopausal, of lower SES and a diet lower in saturated fat. Conclusion: Cluster analysis identified biologically meaningful groups, and allowed for the identification of modifiable risk factors for CM disease.

**805-P****Ability of Waist-to-Height Ratio and Waist Circumference to Identify Metabolic Risk in a Sample of Azorean Adolescents (Portugal)**

Carla Moreira, Rute Santos, Susana Vale, Paula C. Santos, Ana I. Marques, Luisa Soares-Miranda, Jorge Mota *Porto, Portugal*

Background: Several studies found the indexes of abdominal obesity - waist circumference and waist-to-height ratio (WHtR) - were strong predictors of CVD and type 2 diabetes. This study aimed to compare the abilities of these 2 indexes to identify adolescents with high metabolic risk based on receiver operating characteristic curve analysis. Methods: A cross-sectional school-based study - The Azorean Physical Activity and Health Study II, of 517 adolescents (297 girls) aged 15-18y from Azorean Islands was conducted. We measured percentage of fat mass, total cholesterol, high-density-lipoprotein cholesterol (HDL-C), homeostasis assessment model of insulin resistance, triglycerides and, systolic blood pressure. The ratio of total cholesterol/HDL-C was calculated. For each of these variables, a Z-score was computed. The HDL-cholesterol was multiplied by -1. Then, a metabolic risk score was constructed by summing the Z scores of all individual risk factors. High risk was considered when the individual had ≥1SD of this score. Waist circumference and height were used to calculate WHtR. Results: WHtR (AUC=0.807, 95%CI:0.771-0.841) was a slightly better predictor of high metabolic risk than waist circumference (AUC=0.790, 95%CI:0.752-0.824). WHtR cut-offs of 0.55(girls) and 0.49(boys) best identified adolescents with high metabolic risk. Waist circumference cut-off for high metabolic risk were 83 cm in girls (AUC=0.765, 95%CI:0.712-0.812) and 89 cm for boys (AUC=0.826, 95%CI:0.769-0.874). Conclusions: There is little difference in the abilities of WHtR and waist circumference to identify adolescents with high metabolic risk. Both indexes are useful in population health as it identifies adolescents at greater risk of developing metabolic diseases.

**806-P****HbA1c Accurately Tracks Glucose Response During an OGTT Among Healthy, Prediabetic, and Diabetic Volunteers**

Gabriel Q. Shaibi *Phoenix, AZ*; Kelsey Hackett, Andres Monge, Ariana Miller *Tempe, AZ*; Don Wilson *Phoenix, AZ*; Lawrence Mandarino *Tempe, AZ*

Purpose: HbA1c has been endorsed as a means to diagnose type 2 diabetes (T2DM), but whether HbA1c reflects glycemic profiles in non-diabetic subjects has not been determined adequately. Therefore, the purpose of this investigation was to determine the relationship between HbA1c and glucose response to an Oral Glucose Tolerance Test (OGTT) among individuals with T2DM, prediabetes, or normal glucose levels. Methods: Data from 404 Latino individuals (age 33±12 yrs) participating in the Arizona Insulin Resistance Registry were used to assess HbA1c, fasting and 2-hour glucose, and glucose area under the curve (AUC) during a 2-hour OGTT. T2DM was defined as fasting glucose ≥126 mg/dl or 2-hr glucose ≥200 mg/dl and prediabetes was defined as fasting glucose ≥100 mg/dl or 2-hr glucose ≥140 mg/dl. OGTT glucose AUC was assessed by the trapezoidal method using 30-minute sampling time points. Results: HbA1c and glucose AUC were significantly

different between each glycemic phenotype, T2DM (HbA1c=7.4±1.9%, AUC=30046±8163), prediabetic (5.8±0.3%, AUC=20179±2623), normoglycemic (5.3±0.3%, AUC=15524±2404), all  $p < 0.05$ . For the entire cohort, HbA1c was significantly associated with glucose AUC ( $r=0.81$ ,  $p < 0.001$ ). When stratified according to glycemic phenotype, the correlation was stronger within the T2DM group ( $r=0.88$ ,  $p < 0.001$ ), than within either the prediabetic ( $r=0.22$ ,  $p < 0.03$ ) or normoglycemic group ( $r=0.19$ ,  $p < 0.01$ ). Conclusion: HbA1c not only may serve to diagnose T2DM, but also may provide information about glucose response among prediabetic and healthy individuals as well. Prospective studies to examine whether HbA1c can identify individuals at risk for developing T2DM are warranted.

**807-P****Relation of Weight Suppression to Resting Metabolic Rate, Habitual Energy Expenditure and Caloric Intake in College-Aged Women**Eric Stice, Shelley Durant *Eugene, OR*

Recent data indicate that individuals with a current weight that is much lower than their previous highest weight show poorer response to eating disorder treatment and future risk for weight gain. Yet, little is known about mechanisms that explain the predictive effects of weight suppression. We tested the hypothesis that weight suppression is associated with lower resting metabolic rate (RMR), habitual energy expenditure, which is partially based on RMR, and habitual energy intake. A secondary aim was to investigate the impact of using self-reported versus objectively measured current weight on these relations. We assessed RMR and used doubly labeled water to estimate habitual energy expenditure and energy intake with 75 college-aged women. The continuous measure of weight suppression did not show significant inverse correlations with RMR, energy expenditure, or energy intake, as expected. However, there was a marginal inverse correlation between weight suppression and RMR, accounting for 1-2% of the variance, and with energy intake, accounting for approximately 2% of the variance. Interestingly, 15% of the subjects had a negative value for weight suppression, indicating that their retrospective self-reported highest weight ever was actually lower than their objectively measured current weight. When weight suppression was measured using self-report data, the marginal effects observed for RMR and energy intake became non-significant. Results provide support for the thesis that weight suppression leads to a slower RMR and energy intake, but suggest these effects are modest and that the effects for weight suppression may be driven by other factors (a general overeating tendency).

**808-P****Nourishing an Urban Community: Assessing Health Risk Among Public School Students**Susan B. Racette, B. Ruth Clark, M. Leanne White, Nathaniel K. Royer *Saint Louis, MO*

Background: Neighborhood inequity in the availability of healthful food contributes to health disparities in urban populations. Individuals with limited access to healthful food are at greater risk for obesity, diabetes, heart disease, cancer, and premature death. Aim: The aim was to determine the prevalence of obesity, overweight, elevated blood pressure, and low physical fitness among students in an urban public school district. Methods: Students in grades 5-12 underwent assessments of height, weight, resting blood pressure, and physical fitness based on the President's Challenge one-mile endurance run. BMI-for-age, blood pressure, and fitness percentiles were computed using sex- and age-specific criteria. Results: District-wide, 81% of students are Black, 14% are White, and 69% qualify for free/reduced lunch. Of 2,179 students assessed for BMI, 23.7% of students were categorized as obese and 19.0% as overweight. Of 1,015 students with blood pressure measures, approximately one third were categorized as needing further assessment due to high systolic and/or diastolic values. A striking proportion of the 2,902 students with fitness data did not meet the 50<sup>th</sup> percentile endurance fitness benchmark, and a disturbing decline was observed between 5<sup>th</sup> grade and high school. Among 5<sup>th</sup> graders, 50% of females and 62% of males had low fitness (i.e., <50<sup>th</sup> percentile), whereas among 9<sup>th</sup>-12<sup>th</sup> graders, 88% of females and 89% of males had low fitness. Conclusion: Children and adolescents attending urban public schools located in food deserts are at high risk for obesity, hypertension, and poor fitness. School-based initiatives to address these health concerns are essential.

**809-P****Low Bone Mineral Density Found in Overweight and Obese Chilean Adolescents**Estela Blanco *La Jolla, CA*; Marcela Reyes, Raquel A. Burrows *Santiago, Chile*; Suzanna Martinez, Sheila Gahagan *La Jolla, CA*

Background: Osteoporosis, associated with low bone mineral density (BMD), is a major public health problem. Peak bone mass (PBM) is influenced by genetic factors, nutrition, body weight and physical activity with 90% of PBM obtained by age 18 years. Obesity was once believed to protect against low BMD. However, recent research challenges this paradigm. Methods: We assessed 166 adolescents who were part of an iron deficiency anemia preventive trial during infancy. After an overnight fast, we measured anthropometry and dual energy X-ray absorptiometry (DXA). Using World Health Organization growth standards, we determined body mass index (BMI) percentile. Femoral neck and lumbar spine BMD were categorized as low BMD, Z-score  $\leq -1$ , and very low BMD, Z-score  $< -2.5$ . Results: Participants were 16- to 17-yr old, 52% female, 4% underweight, 33% 85<sup>th</sup> BMI, average BMI 61<sup>st</sup> %ile. Criteria for low BMD were met by 25% and for very low BMD by 1%. Bone density Z-score and BMI %ile were correlated ( $r=.52$ ,  $p < 0.001$ ). Female gender ( $p < 0.01$ ) and BMI  $< 85^{\text{th}}$  %ile ( $p < 0.01$ ) were associated with risk for low BMD. Nonetheless, 11% ( $n = 6$ ) of the overweight ( $n=4$ , 2 boys and 2 girls) and obese ( $n=2$ , 2 girls) participants met criteria for low BMD. Conclusions: In our sample of low-to middle-income Chilean adolescents, low BMD was prevalent and did not spare overweight and obese girls and boys. Future research should explore how age of onset of adiposity and fat distribution influence the relationship between adiposity and low BMD.

**810-P****Optimal Waist Circumference Thresholds to Identify Cardiometabolic Risk in African American and White Adults: Receiver Operating Characteristic Curve Analyses**Peter T. Katzmarzyk *Baton Rouge, LA*

Background: The most common waist circumference (WC) thresholds used to define abdominal obesity were derived in European populations. The purpose of this study was to derive optimal WC thresholds for the identification of cardiometabolic risk among white and African American (AA) adults. Methods: The sample included 2099 white women, 1790 AA women, 1951 white men, and 643 AA men aged 18-64 years. WC was measured at the midpoint between the lowest rib and the iliac crest. Elevated cardiometabolic risk was determined by the presence of  $\geq 2$  risk factors [systolic/diastolic blood pressure  $\geq 130/85$  mmHg, fasting glucose  $\geq 100$  mg/dL, triglycerides  $\geq 150$  mg/dL, HDL-cholesterol  $\leq 40$  mg/dL (men) or  $\leq 50$  mg/dL (women)]. Receiver Operating Characteristic curves were used to identify optimal WC thresholds for the prediction of cardiometabolic risk in each sex-by-race group. Results: WC was a significant predictor of cardiometabolic risk in all sex-by-race groups ( $p < 0.0001$ ). The area under the curve (AUC) values were 0.784 in white women, 0.753 in AA women, 0.758 in white men, and 0.769 in AA men. The optimal WC thresholds were 91.9 cm in white women, 96.8 cm in AA women, 99.4 in white men, and 99.1 cm in AA men. The sensitivities and specificities at the optimal thresholds ranged from 0.684 to 0.710 and 0.685 to 0.710, respectively. Conclusions: Optimal WC thresholds for identifying cardiometabolic risk are higher in men than in women. There are no apparent race differences in men; however, optimal WC values are approximately 5 cm higher in AA compared to white women.

**811-P****Prevalence of Abdominal Obesity and Its Relationship With Hypertension Among the Rural Elderly in India**N. Arlappa, A. Laxmaiah, N. Balakrishna, R. Harikumar, Ch. Galreddy, R. Mallikarjuna, K. Sharadkumar, M. Ravindranath, G.N.V. Brahmam *Hyderabad, India*

Background: Studies to show the relationship between hypertension and obesity in elderly were scanty in India. Methods: A community based cross-sectional study was carried out with the objective to assess the prevalence of abdominal obesity and its relationship with hypertension among the elderly residing in rural India. A total of 3,133 (Men: 1677; Women: 1456) elderly were covered from 1,080 villages. Waist Circumference (WC) was measured nearest to 0.1 cm. WC of  $>90$ cm for men and  $>80$ cm for women were

considered to determine abdominal obesity. Blood pressure was recorded using standard mercury sphygmomanometer. Systolic blood pressure of  $\geq 140$  mmHg and/or diastolic blood pressure of  $\geq 90$  mmHg and/or those were on medication for hypertension was considered as hypertensives. Results: The prevalence of abdominal obesity and hypertension was significantly ( $p < 0.001$ ) higher among elderly females (22.9% and 53.3%) as compared to males (13.2% and 47.3%). In general, the mean WC was significantly ( $p < 0.001$ ) higher among hypertensive men and women, as compared to normotensives. The abdominal obesity was highly correlated with the systolic (Men:  $r = 0.192$ ; Women:  $r = 0.205$ ) and diastolic (Men:  $r = 0.177$ ; Women:  $r = 0.172$ ) blood pressures. Abdominal obesity had twice the risk of having hypertension among both elderly men (OR=1.6; CI: 1.2-2.1) and women (OR=2.6; CI: 2.0-3.3) as compared to non-obese. Conclusion: The prevalence of abdominal obesity and hypertension among elderly was public health concern in India. Abdominal obesity has strong correlation and is significant risk factor for hypertension. Therefore, WC is a useful anthropometric measurement for screening cardiovascular risk factors among elderly.

### 812-P

#### Waist Circumference Can Be Used to Predict Metabolic Syndrome in Adolescents of Ho Chi Minh City, Vietnam

Trang H. Nguyen Hoang, Hong K. Tang *Ho Chi Minh City, Vietnam*; Michael J. Dibley *Sydney, Australia*

Objective: To identify principal components of risk variables associated with metabolic syndrome (MetS) in adolescents of Ho Chi Minh City (HCMC), Vietnam. Methods: A cross-sectional study was conducted on 617 adolescents (285 males and 332 females) studying in secondary schools in HCMC in 2007. Height, weight, waist circumference (WC) and blood pressure were measured and fasting blood tests including total cholesterol, HDL-c, LDL-c, triglycerides, glucose were also collected. MetS was defined as having three or more of the followings: triglycerides  $\geq 1.24$  mmol/L, HDL  $\leq 1.03$  mmol/L, LDL  $\geq 2.6$  mmol/L, fasting glucose  $\geq 6.1$  mmol/L and systolic/diastolic blood pressure  $\geq 90$ th percentile for gender, age and height. Receiver operating characteristic analysis was used to identify the optimal WC percentile threshold to predict elevated cardiovascular risk. Principal component analysis was applied to define the main components of risk variables associated with MetS. Results: Optimal cut-off values of WC percentile were 75.3cm (95%CI: 64.55, 82.06) in boys, 65.5 cm (95%CI: 58.77, 74.12) in girls. Factor analysis revealed three uncorrelated factors that cumulatively explained 62.7 % of the observed variables of MetS. The three factors identified were obesity (including BMI, WC, and LDL-c), hypertension (systolic and diastolic blood pressure) and dyslipidemia (including Triglyceride, HDL). Conclusion: Not only one physiological mechanism could account for the clustering of risk variables of metabolic syndrome in adolescents of HCMC. The early detection using the optimal WC cut-off values is necessary to track and prevent effectively the occurrence of this syndrome.

### 813-P

#### Sex But Not Race Differences in the Prevalence of CT Measured Fatty Liver Disease in European American and African American Participants of the NHLBI Family Heart Study

Kari E. North, Mariaelisa Graff, Nora Franceschini *Chapel Hill, NC*; Mary F. Feitosa *Saint Louis, MO*; J. Jeffrey Carr *Winston-Salem, NC*; Penny Gordon-Larsen *Chapel Hill, NC*; Mary K. Wojczynski, Ingrid B. Borecki *Saint Louis, MO*

Fatty liver disease (FLD) is characterized by increased intrahepatic triglyceride content with or without inflammation and fibrosis and has been associated with obesity, diabetes, insulin resistance, and alcohol ingestion. Liver attenuation (LA) (Hounsfield Units, H.U.) by computed tomography (CT) is a validated noninvasive quantitative measure of liver fat. Although the epidemiology of FLD has been largely unexplored, previous studies demonstrated a differential prevalence of FLD by race and sex. We examined race- and sex-prevalence differences and its predictors on the distribution of LA in EA and African American (AA) participants of the NHLBI Family Heart Study. A total of 1253 (1068 EA, 185 AA) and 1483 (1153 EA, 330 AA) men and women, respectively, were measured for LA and abdominal tissue volume. LA (adjusted for age, phantom, and center) was the dependent variable in linear mixed models (to control for family relatedness) that tested for prevalence differences by race and by sex. Independent explanatory variables included the additive effects of a PNPLA3 variant,

body mass index, visceral tissue volume, subcutaneous tissue volume, alcohol consumption, triglyceride concentration, and insulin resistance. Mean LA varied significantly by sex, [(men)  $-57.76 \pm 10.03$  HU and (women)  $60.03 \pm 10.91$  HU,  $p = 0.0002$ ], but not by race. LA was associated with age, genotype, body mass measures, and triglycerides in women and additionally for alcohol consumption in men. In contrast to previous literature, our study findings are suggestive of important sex differences in LA in both EA and AA populations.

### 814-P

#### Does Fat Fuel the Fire: Investigating the Inter-Relationships Between Adipose Tissue, Bone, and Markers of Inflammation

Lynae J. Hanks, Krista Casazza, Jessica Alvarez, Jose R. Fernandez *Birmingham, AL*

Markers of inflammation (MOI) have been reported to influence both systemic inflammation and bone health in adults, with reports of a positive association between inflammation and bone resorption. Adipose, a well-established source of MOI, has also been linked to bone. In children, the interrelationships between adiposity, inflammation and bone is unclear, warranting investigation of interactions as an opportunity for developing preventive strategies of long-term bone health. The objective of this study was to evaluate the relationship between MOI (i.e. CRP, TNFR2, IL-6) and bone mineral content (BMC) and to determine the contribution of fat deposition/distribution in peri-pubertal (Tanner stage  $\leq 3$ ) children. Fifty-four children (59% male) 7-12y participated. Body composition was evaluated by DXA, and MOI and insulin sensitivity ( $S_i$ ) were obtained during an IVGTT. Multiple linear regression analysis was used to evaluate the relationship between MOI and BMC in models controlling for total fat, percent fat, and abdominal adipose tissue, respectively. Models were also stratified individually by sex and median  $S_i$ . TNFR2 was inversely associated with BMC in all models. In boys, TNFR2 was inversely associated with BMC, and in girls IL-6 was inversely associated with BMC, and total and percent fat moderated both relationships. Further, individuals with lower  $S_i$  had lower BMC. Our results suggest a potential inhibitory role of inflammation on bone as well as a negative impact of adiposity. These relationships are particularly salient during this period of rapid bone acquisition. Future investigations are warranted to investigate the contribution of sex and metabolic parameters to these relationships.

### 815-P

#### Pleiotropic Effects of Serine Palmitoyltransferase Subunit 2 (SPTLC2) on Fatty Liver Disease and Total Abdominal Adipose Tissue Volume or Extreme Obesity in the NHLBI Family Heart Study (FHS)

Mary F. Feitosa, Mary K. Wojczynski *Saint Louis, MO*; Kari E. North, Nora Franceschini *Chapel Hill, NC*; Michael A. Province *Saint Louis, MO*; J. Jeffrey J. Carr *Winston-Salem, NC*; Ingrid B. Borecki *Saint Louis, MO*

Nonalcoholic fatty liver disease (NAFLD) presents as a disease spectrum from fatty liver (steatosis), to nonalcoholic steatohepatitis, to fibrosis. Obesity is a major risk factor for NAFLD. CT measured liver attenuation (LA) is inversely related to fat in the liver and is inversely correlated with CT measured volume of total abdominal adipose tissue (TAT,  $r^2 = -0.34$ ) and extreme obesity (EOB,  $r^2 = -0.42$ ) in the FHS. A correlated meta-analysis approach can improve power to detect variants that have pleiotropic effects on LA and its correlated traits. We investigated LA with TAT and EOB, in 2,679 subjects of European descents using genomewide (GW) association analysis of  $\sim 2.5$  million imputed SNPs. We found evidence for association of the UTR3-SPTLC2 variant (rs10132095) with LA-TAT ( $p = 5.4E-8$ ) and LA-EOB ( $p = 2.6E-8$ ). The marginal results for each trait with this variant did not reach GW significance (LA:  $p = 2.1E-5$ , TAT:  $p = 1.2E-4$ , and EOB:  $p = 6.5E-5$ ), supporting the utility of this analytic approach. SPTLC2 encodes a base subunit of serine palmitoyltransferase that is the key enzyme in sphingomyelin (SM) biosynthesis. SM is one of the major lipid components of plasma lipoproteins, and liver is the major site for plasma lipoprotein biosynthesis, secretion, and degradation. Sphingolipids (including ceramide) have also been implicated in the pathogenesis of obesity, insulin resistance and cardiovascular disease. SPTLC2 expression is involved in the pathway of high fat diet and increased ceramide levels in the adipose tissues and plasma in mice. Our findings suggest that SPTLC2 may in part explain the association between NAFLD and adiposity.

**816-P****Independent Effects of Adiposity and Vitamin D Status on Cardiometabolic Risk in Schoolchildren**

Jennifer Sacheck, Elizabeth Goodman, Virginia Chomitz, Aviva Must, Christina Economos *Boston, MA*

**Background:** Although obesity is associated with serum 25-hydroxyvitamin D (VitD) deficiency and both conditions are linked to cardiometabolic risk in adults, these relationships have not been firmly elucidated in children. **Methods:** We examined the relationships amongst adiposity, serum VitD, and cardiometabolic risk factors in 276 racially diverse schoolchildren (mean age=11.4 ± 1.6 yr) from Boston during February-early April when serum VitD levels are low. BMI, serum VitD, and blood lipids were measured. Separate multiple linear regression analyses controlling for age, gender, ethnicity, and socioeconomic status were run for the following dependent variables: triglycerides, HDL-C, LDL-C, total cholesterol. **Results:** 45% had BMI>85th percentile. Almost all were VitD insufficient (96.6%; serum VitD≤30 ng/mL), 76.4% of whom were VitD deficient (serum VitD≤20 ng/mL). Serum VitD range was 6.6-38.3 ng/mL; mean=16.7±5.5 ng/mL. Multiple linear regression revealed that adiposity was not associated with serum VitD. BMI was associated with elevated triglycerides and low HDL-C (B=0.07, P<0.01 and B=-4.7, P<0.01, respectively). Lower serum VitD was marginally associated with elevated cholesterol and LDL (B=-0.5, P=0.07 and B=-0.46, P=0.07, respectively). **Conclusions:** VitD insufficiency/deficiency is nearly universal among schoolchildren living in northern latitudes during late winter. Furthermore, the lack of any strong association between serum VitD and adiposity as well as cardiometabolic risks may be due to the narrow range of serum VitD in this population caused by the high level of VitD deficiency. Future studies should examine the effects of improving VitD status in children at high risk of deficiency and the resultant impact on cardiometabolic risk factors.

**817-P****Metabolic Syndrome and Body Composition Improvement in Chilean Women After Weight Loss With Caloric Restriction Diet**

Yaisy Picrin, Lydia Lera, Valquiria Couto *Santiago, Chile*

**Background:** Several studies have demonstrated that obesity and fat mass are associated with Metabolic Syndrome (MS). Weight loss can improve metabolic indexes. The aim of this study is to evaluate metabolic and body composition changes through weight loss with low-carbohydrate diet in Chilean women. **Methods:** Cross-sectional study of 475 women was performed to study the influence of MS and obesity. 155 women (mean age: 49.1±13.0 years) were selected from these patients participating in weight loss treatment with low-carbohydrate diet under weekly medical supervision over 3 months. Waist circumferences (WC), systolic and diastolic blood pressures, concentrations of total cholesterol (TChol), high-density cholesterol (HDL-Col), triglycerides (TG), and glucose were taken with overnight fasting. Body composition was measured by Dual energy X-ray absorptiometry (DXA) and bioelectrical impedance (BIA). APT3 criteria were used to classify metabolic syndrome. All indexes were measured before and 3 months after treatment. **Results:** Body Mass Index (BMI) (28.1±4.1 vs 25.0±3.5 kg/m<sup>2</sup>; p<0.0001) and waist circumferences (92.5±10.7 vs 83.0±10.8 cm; p<0.0001) diminished. Fat mass was significantly reduced (32.8±7.4 vs 31.6±7.1 kg; p = 0.0430) while lean mass values showed no statistical differences (35.6±4.4 vs 34.9±6.3 kg; p = 0.2576). Patients with MS diminished less fat (android fat: 41.7±7.6 vs 36.9±9.5; gynoid fat: 43.4±6.1 vs 42.9±3.8) than those without MS. The biochemical markers TChol (214.9±52.3 vs 197.8±41.3 mg/dl; p=0.0315) and TG (157.2±100.8 vs 123.9±92.5 mg/dl; p = 0.0355) decreased significantly. **Conclusion:** Our studies suggest that weight loss using low-carbohydrate diet, improves body composition and metabolic disorders.

**818-P****The Additive Effects Between PPAR $\gamma$  Gene and Childhood Growth on Insulin Resistance Development at Three Years of Age**

Jungwon Min, Sujin Cho, Youngju Kim, Hwayoung Lee, EunAe Park, Eunhee Ha, Hyesook Ha *Seoul, Korea*

**Background:** The PPAR $\gamma$  has a key role in adipocyte differentiation and susceptibility to insulin sensitivity. The Ala allele was related to body composition regulation from utero to adulthood. Because early weight change also shows its association with insulin resistance (IR)

development, we hypothesized that PPAR $\gamma$  gene and early weight change may have additive effects on childhood IR risk. **Methods:** The Pro12Ala polymorphism was genotyped and fasting glucose and insulin levels were measured in 324 subjects who participated in the Korean birth cohort of Ewha Womans University (2005-08). Body composition changes were recorded from medical chart and prospective follow-up investigation. The different IR levels in Pro12Ala polymorphisms and accelerated growth were compared with ANOVA and logistic regression model. **Results:** There is no difference in weights at birth or at three years of age and weight change according to the Pro12Ala polymorphism. Those who experienced accelerated growth had higher level of IR indices. With the combination of PPAR $\gamma$  gene and accelerated growth, the accelerated Ala allele group showed the highest level of IR (HOMA: 1.2mmolXuU/mL, Insulin: 5.6uL/mL) and normal Pro allele group had the lowest IR (HOMA:0.8, Insulin: 4.3). The odds ratio of 90 percentile of HOMA was 7.6 in accelerated Ala allele group, compared to the normal Pro allele group. **Conclusions:** Although three years is early years, children already showed their additive effects between PPAR $\gamma$  gene and accelerated growth in IR development. It suggested that possible gene-early growth interactions in IR.

**819-P****Leptin Is Independently Associated With Smaller Left Ventricular Mass and Volume: The Multi-Ethnic Study of Atherosclerosis**

Matthew Allison *La Jolla, CA*; Robyn McClelland *Seattle, WA*; Joao Lima *Baltimore, MD*; Mary Cushman *Colchester, VT*; David Bluemke *Bethesda, MA*; Joseph Polak *Boston, MA*; Michael H. Criqui *La Jolla, CA*

**Introduction:** Adipokines have been linked to cardiovascular disease (CVD). We evaluated the associations between 4 adipokines and measures of left ventricular (LV) structure and function. **Methods:** 1968 Multi-Ethnic Study of Atherosclerosis (MESA) subjects underwent magnetic resonance imaging (MRI) to determine LV mass (LVM), volume (LVV), ejection fraction (LVEF), cardiac output (CO). To control for body size, LV mass and volume were expressed as a percentage of their predicted value based on height, weight and gender. Blood was analyzed for adiponectin, leptin, tumor necrosis factor – alpha (TNF) and resistin. **Results:** Mean age was 62. Half were male while 40% were White, 26% Hispanic, 21% African American and 13% Chinese American. There were no significant associations between the LV measures and adiponectin, TNF and resistin. However, compared to the lowest quartile of leptin and after adjustment for age, gender, ethnicity, traditional and novel CVD risk factors, the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> quartiles of leptin were associated with lower levels of LVM (-4.8, -7.9 and -11.9%, respectively; p < 0.01 for all) and LVV (-7.6, -9.3 and -10.5%, respectively; p < 0.01 for all). There were no significant interactions between leptin and ethnicity for LVM or LVV. There were also no significant associations between leptin and LVEF or CO, although among African Americans, higher leptin was associated with significantly higher CO. **Conclusion:** In MESA, the pro-inflammatory adipokine leptin appears to be relevant to measures of LV structure and function independent of CVD risk factors.

**820-P****Metabolic Syndrome, Cultural Involvement, and Health Related Quality of Life in American Indian Parents/Caregivers**

Ronald J. Prince, Alexandra Adams, Kate A. Cronin, Tara L. LaRowe *Madison, WI*

**Background:** American Indians experience very high rates of type 2 diabetes and cardiovascular disease. Metabolic syndrome (MetS) greatly increases the risk for both diseases. Research has shown that MetS has impacts on health related quality of life (HRQoL). However, cultural differences also impact the measurement of HRQoL. We examined how both affected HRQoL in a group with high rates of MetS and unique cultural influences. **Methods:** 91 child caregivers (88 women; mean age 33) completed measures including fasting glucose and lipid levels, B/P and waist circumference to diagnose MetS using accepted criteria. Participants also completed the SF-12v2, a widely used measure of HRQoL, and a 20-item cultural inventory about cultural attitudes and participation in cultural events. The SF-12 yields primary Physical and Mental component scores and 8 subscale scores. The cultural inventory was factor analyzed yielding 4 factor subscales and a total score for self-

rated cultural involvement. Results: 36% of participants had MetS. Those with MetS had significantly ( $P<.001$ ) lower scores on the SF-12 Physical component score (50.8 vs. 43.8) and 3 of 4 physical subscale scores but no differences in Mental component score (44.9 vs. 43.9). High vs. low scorers on the cultural involvement scale scored significantly ( $P<.001$ ) higher on the SF-12 Mental component score (50.5 vs. 40.4) but no difference on Physical (44.6 vs. 48.2). Discussion: Because identification with culture seems to have a positive influence on at least one aspect of HRQoL, it may be important to consider traditional culture in treatment and prevention efforts.

**821-P****One-Year Changes in Body Mass Index Are Related With Changes in Blood Glucose and Blood Pressure in Mexican Adolescents and Young Adults**

Itzel Vazquez *Champaign, IL*; Tracy Flood, Yingying Wang, Margarita Teran-Garcia *Urbana, IL*; Celia Aradillas-Garcia, Eduardo Medina-Cerda, Juan Vargas *San Luis Potosi, Mexico*; Flavia Andrade *Champaign, IL*

Purpose: The objective of this study was to assess weight changes over time among Mexican college applicants and to explore the effects of weight gain on blood pressure and blood glucose over time. Background: In American college students, the transition from high school to college is associated with weight gain. However, it is unclear whether a similar pattern would be found in Mexico. Methods: We used longitudinal data from 1507 adolescents and young adults aged 16 to 21 years who applied to The University of San Luis Potosí (UASLP) in 2008 and 2009. Weight, height, waist circumference, body mass index (BMI), blood pressure (systolic [SBP] and diastolic [DBP]) and fasting glucose were measured. Results: Over 1-year, weight gain was found in males (64.3%) and females (59.9%); few students had no change in BMI (males: 5.5%; females: 3.1%); and about a third lost weight (males: 30%; women 36.6%). Logistic regression showed that increases in BMI were associated with an increase in glucose levels over time for females (OR=1.14; 95%CI, 1.03-1.26,  $p$ -value=0.006) but not for males. Also, we found that increases in BMI were associated with changes in SBP in males (OR=1.23; 95%CI, 1.09-1.40,  $p$ -value=0.002) and females (OR=1.21; 95%CI, 1.08-1.35,  $p$ -value<0.0001) but not DBP. Conclusion: Weight gain in this population is of particular concern because changes in BMI in childhood and adolescence have been linked to an increased risk of chronic diseases in adults such as cardiovascular disease and diabetes, the leading causes of death in Mexico and America.

**822-P****BMI and Risk of Musculoskeletal Injuries Among Army Trainees Meeting Body Fat Standards**

Nadia Urban *Silver Spring, MD*, Sheryl A. Bedno *Bethesda, MD*, Marlene E. Gubata, Bin Yi, David N. Cowan, David W. Niebuhr *Silver Spring, MD*

Purpose: As part of a larger study evaluating the risk of musculoskeletal injury (MSI) associated with exceeding body fat percent (BF%) standards among men entering the US Army, we investigated the effect of body mass index (BMI) category on the incidence of MSI among men meeting BF% standards. Methods: We evaluated first-time applicants to the US Army entering February 2005-September 2006, using four BMI categories: BMI  $\leq$ 18.5 (underweight); 18.5-24.9 (normal); 25-29.9 (overweight) and  $\geq$ 30 (obese). Age and tobacco use at time of entry were also recorded. The outcome was MSI to the lower extremity occurring during the first 90 days of service. The measure of association between BMI and injury was the hazard ratio (HR), and only significant findings are reported. Results: Among 9403 study participants, 2759 (29%) incurred an injury within the first 90 days. Obese and underweight were significantly associated with injury (HR=1.17 and HR=1.33, respectively). No association was observed in the overweight category. Those 20-24 and  $\geq$ 25 years-old were at increased risk compared to those 18-19, with HR=1.24 and HR=1.62, respectively. Smokers were also at increased risk, with HR=1.26. Conclusions: This research indicates that both underweight and obese men were at increased and similar risk of musculoskeletal injury to a lower extremity during the first 90 days of military service. Age and tobacco use were also significant predictors of injury. These findings have potential utility in targeting high-risk individuals for intervention efforts.

**Weight Change****823-P****Body Mass Trajectories Through Adulthood: Analysis of the National Longitudinal Survey of Youth 1979 Cohort (1981-2006)**

Truls Østbye *Durham, NC*; Rahul Malhotra *Singapore*; Richard L. Landerman *Durham, NC*

We sought to identify meaningful Body Mass Index (BMI) trajectories from age 18 to 49 using group-based latent trajectory modeling based on information from 9681 individuals from the National Longitudinal Survey of Youth 1979. Risk factors (gender and race/ethnicity) for trajectory group membership, and (time varying) modifiers of trajectory shape (highest grade completed, years of urban living, years in employment, years in poverty and years married) within each group were assessed. Association between the trajectory groups and a set of important health outcomes (e.g. diabetes, hypertension) in midlife was ascertained. Four body mass trajectory groups, 'normal weight' (NW) (membership: 35.0%), 'overweight' (OW) (41.2%), 'late adulthood obesity' (LO) (19.7%) and 'early adulthood obesity' (EO) (4.2%) were identified. Males and Blacks had significantly higher odds of being in the OW, LO and EO groups relative to NW. Higher educational level and more years married were associated with "lowering" of the trajectory in each group. There was a decline in SF-12<sup>®</sup> physical component scores, and a strong increase in the prevalence of a range of adverse health outcomes in midlife with increasingly higher trajectory group, from NW to EO. Identifying a person as belonging to one of these four groups early may provide the individual and his or her health care providers an opportunity to monitor and intervene early with behavioral or other interventions tailored to the group.

**824-P****Longitudinal Study of Body Weight and Fat Changes in Boys and Girls: Who Is Gaining and Who is Not?**

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Cross-sectional studies have reported significant temporal increases in prevalence of childhood obesity in boys and girls and various racial/ethnic groups. Recently, Ogden et al (2010) using NHANES data concluded that the increased prevalence of obesity has slowed except in boys with BMI  $\geq$  97<sup>th</sup> percentile. Furthermore, two recent childhood obesity prevention studies (using longitudinal designs) reported that overweight/obese children lost body weight/fat and non-overweight children gained body weight/fat. This investigation tested the hypothesis that overweight children are losing body weight/fat and non-overweight children are gaining body weight/fat using a longitudinal research design without an obesity prevention program. The participants were 451 children enrolled in 4<sup>th</sup> to 6<sup>th</sup> grades. Height, weight, and body fat (using body impedance analysis) were measured at Month 0 and Month 28. Higher BMI percentile scores and percent body fat at baseline were associated with larger decreases in BMI scores and percent body fat after 28 months. This relationship was observed in both genders and in white and African-American children. The mean BMI percentile for white boys and girls and African-American boys was stable over the 28 month study period; whereas the mean BMI percentile of African-American girls increased ( $M = 3.3 \pm 1.7$ ;  $p < 0.05$ ). White and African-American girls gained body fat during the study period, but African-American girls gained more body fat ( $p < 0.005$ ). Results support the hypothesis that overweight children are losing body weight/fat and non-overweight children are gaining body weight/fat. Longitudinal studies of body weight/fat changes in representative samples are needed.

**825-P****Young Adult Weight Predicts Weight Trajectory Through Adulthood: A Latent Class Growth Modeling Approach**

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Defining patterns of weight over time may provide insight into characteristics leading to future weight gain. Latent class growth modeling (SAS procedure PROC TRAJ) was used to define subgroups of weight change in adult members of the Gila River Indian Community participating in at least 4 non-diabetic, non-pregnant biennial health exams ( $n=1288$  (458 M; weight =  $78.1 \pm 19.9$  kg, mean $\pm$ sd)), with an initial visit between the ages of 18-24 yrs (mean =  $20 \pm 2$ ). The best model defined 6 groups

with starting weights of 54.6±67 (n=146), 65.0±7.5 (n=334), 77.4±8.7 (n=350), 91.3±9.7 (n=289), 107.3±12.3 (n=130), and 133.6±18.5 kg (n=39) ( $p<0.0001$ ). Weight change over time (mean follow-up: 17±8 yrs) increased in proportion to initial weight ( $p<0.0001$  across groups) with greater rates of increase/year in the heavier groups (kg/yr: 0.7±0.5, 1.1±0.8, 1.2±1.0, 1.5±1.6, 2.1±1.6, and 2.7±1.8;  $p<0.0001$ ). A subset of 136 individuals (63 M; 92.2±26.4 kg; 20±2 yrs; 33±10% body fat) who were evenly distributed across the growth trajectories had 24h energy expenditure (EE) and substrate oxidation measurements in a respiratory chamber within 5 years of the initial exam. Adjusted EE, RQ, and substrate oxidation were not predictors of weight gain trajectory. In conclusion, non-diabetic young adults with lower body weight are more likely to maintain their weight throughout adulthood. This was unrelated to 24h EE or substrate oxidation indicating food intake and/or physical activity are likely to be the primary factors in weight change. Interventions to prevent excessive weight gain prior to early adulthood may alter subsequent weight trajectories.

**826-P****Energy Expenditure and Holiday Weight Gain Among 40-69 Year Old Men and Women in the OPEN Study**

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Background: Recent research suggests that a significant proportion of average annual body weight (BW) gain in US adults (~0.5 to 1kg/y) may result from modest episodes of positive energy balance during fall/winter holiday season. We tested whether holiday weight gain was reduced in participants with high total energy expenditure (TEE). Methods: In a retrospective secondary analysis,  $\Delta$ BW from mid-September/mid-October 1999 to mid-January/early-March 2000 was analyzed by sex, age, and BMI in 443 men and women aged 40-69y. TEE was measured by doubly labeled water. Residual TEE was calculated after linear adjustment for age, height, and BW. Results: 73% of all participants gained >0.1kg, with 19% gaining 2kg, over an average of 107±7d. Men gained more BW (1.1±1.6kg; n=242) than women (0.7±1.5kg; n=201) ( $p<0.01$ ). Men with an initial BMI  $\geq 30$ kg/m<sup>2</sup> gained more BW (1.5±1.9kg; n=68) than men with a BMI 19<25kg/m<sup>2</sup> (1.0±1.2kg; n=56) or 25<30kg/m<sup>2</sup> (0.9±1.5kg; n=118) ( $p<0.05$ ). There was no difference in  $\Delta$ BW between BMI categories for women, or between age and sex subgroups. There were no correlations between  $\Delta$ BW and TEE or TEE residuals. Residual TEE ranged from -774 to 1813 kcal/d, with a median (IQR) of -36 kcal/d (-231 to 191 kcal/d). Conclusion: Weight gain was greater among men with higher BMIs. A higher adjusted TEE was not protective against BW gain suggesting interventions targeting the winter holiday quarter to prevent excess BW gain in older men and women should focus on diet vs. increased activity levels.

**827-P****Healthy and Unhealthy Weight Loss Practices Used By College Students in New York City**

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Objective: The purpose of the study is to collect information from college students in New York City to identify healthy and unhealthy weight loss practices used for weight control and the frequency of their use. Participants: The target population was community college students from South Bronx, New York, 352 answered the survey instrument, mostly females (82%), Hispanic/Latinos (45%) between the ages of 20 and 39 years old (78.7%). From those 228 (64.8%) stated being on a special diet to lose weight during the last twelve months, composing the study sample. Data Analyses: Descriptive and inferential statistics were used. Pearson Correlations used to analyze relationships between background characteristics and dieting practices. Results: 228 students (64.8%) reported tried to lose weight during the past year. Healthy weight loss practices used most often were: exercising more (53.1%), eating a little less food (44.1%), and avoiding sweets and junk food (48.8%). Unhealthy weight loss practices used were using diet pills (22.5%), taking laxatives (18%), hardly eating at all or fasting (19.3) or throwing up after eating (8%). Conclusions and Implications: Most adults choose weight loss practices that are reasonable or adequate, but unhealthy behaviors are not uncommon. A better understanding of the weight loss practices used among college students is useful for clinicians and nutritionists in the development of health prevention and weight management treatment programs.

**828-P****Associations Between Lability in Externalizing Behavior and Weight Gain From Age 2 to 15 Years**

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Background: Externalizing behavior (e.g., conduct disorder symptoms) has been associated with relative weight and weight status in childhood and adolescence. Objective: The objective of this report was to determine whether occasion-to-occasion changes in externalizing behavior (lability) was related to weight gain from early childhood (age 2) through mid-adolescence (age 15). Methods: Longitudinal data were drawn from the National Institute of Child Health and Human Development's Study of Early Child Care and Youth Development. Data were available for a total of 1,216 families, collected when children were ages 2, 3, 5, 7, 9, 11, 12 and 15 years. Results: Initial BMI and rate of BMI change over the 13-year period were not related to children's average levels of externalizing behavior, but were both positively, and significantly related to the extent of lability in externalizing behavior, as measured by both within-person standard deviations or range of scores. That is, children characterized by instability in their externalizing behaviors exhibited greater gains in BMI from age 2 to 15 years compared to their more stable peers, controlling for both initial BMI and average levels of externalizing. This effect held constant after adjusting for SES (income-to-needs ratio), mothers' level of depression, and self-regulation ability (self-control at 36 months); the final model accounted for 46% of the variance in BMI gain over the 13-year period. Conclusions: Within-person variability in externalizing behavior predicts weight gain from early childhood through adolescence. There is a need to develop a better understanding of the mechanisms by which this relation exists.

**829-P****Effectiveness of a Publically Funded Weight Management Clinic**

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Background: Despite the remarkable increase in obesity, weight management is still not widely available outside commercial weight loss programs. In this analysis we examine the effectiveness of a publicly funded referral-based weight management clinic in Ontario, Canada. The clinic uses a multidisciplinary team approach that includes nutritionists, behavioural therapists, exercise specialists and internal medicine physicians. Methods: Clinical data was analysed from consecutive consenting patients who were referred to the clinic between Jan 2007 and Jan 2010 and attended the clinic for at least 3 months (mean 5.4 ± 4.7 months, 8.1 ± 6.2 visits). Results: A total of 1085 patients (age: 49.3 ± 12.5 y; BMI: 40.5 ± 8.1 kg/m<sup>2</sup>; 77.6% female) were seen during the observation period. Comorbidities occurred at the following rates; type 2 diabetes 21.2%, hypercholesterolemia 32.6%, hypertension 44.9% and metabolic syndrome 68.8%. On average patients reduced their weight by 4.2 ± 7.1 kg (3.5 ± 6.8%), with 32.2% attaining a weight loss of 5% or greater, and 9.2% attaining 10% weight loss. There were no bariatric surgery patients in this sample. The number of clinic visits was positively correlated with weight loss. ( $P<0.0001$ ). Conclusion: Our results suggest that one third of participants were able to lose a clinically significant amount of weight in a publicly funded specialist weight management clinic. These numbers are comparable to those reported in other behavioural and medical weight management programs. As expected, greater patient contact was associated with greater weight loss. The long-term impact of this program and its cost-effectiveness remain to be explored.

**830-P****The Role of Change in Conscientiousness in Successful Weight Loss**

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Background: Conscientiousness, the propensity to be self-controlled, responsible, and, industrious, has been linked to several health behaviors as well as obesity. However, data are lacking examining the relation of conscientiousness and weight loss. This study examined whether conscientiousness and change in conscientiousness predict successful weight loss. We also explored the relationship between conscientiousness and dietary restraint, a measure of self-control specific to eating behavior, and whether

restraint mediated the effect conscientiousness on weight loss. **Methods:** Participants ( $n = 41$ ,  $BMI = 36.0 \pm 3.8$ ,  $age = 39.2 \pm 9.5$ , 79% female, 65% Caucasian) were enrolled in a behavioral weight control intervention that included a 3-month weight loss phase followed by a 6-month maintenance phase. **Results:** 76% of participants were successful at weight loss defined as  $\geq 7\%$  loss of baseline weight. Conscientiousness at baseline did not predict successful weight loss. However, from baseline to 3 months, participants who successfully lost weight showed an increase in the self-control facet of conscientiousness compared to no change among unsuccessful participants ( $p < .05$ ). Conscientiousness and dietary restraint were significantly correlated ( $r = .45$ ), and dietary restraint mediated the effect of change in self-control on successful weight loss. **Conclusions:** Engagement in the behavioral change intervention with successful weight loss was associated with an increase in the self-control aspect of conscientiousness. The impact of enhanced self-control on weight loss was accounted for by an increase in dietary-specific control. These findings support the neo-socioanalytic model of personality which identifies personality change as a mechanism of positive health outcomes (Roberts & Mroczek, 2008). Supported by R01DK080090.