JOURNAL OF WOMEN'S HEALTH
Volume 17, Number 8, 2008

DOI: 10.1089/jwh.2008.AC03

BIRCWH POSTER ABSTRACTS

P-1: Gender and Cue-Induced Imaging in Nicotine Dependence

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Background: Tobacco dependence remains a significant public health concern. In the United States, cigarette smoking continues to be the leading preventable cause of mortality, accounting for about one out of every five deaths. Exposure to cues associated with smoking results in behavioral, physiological, and subjective effects, including craving. Smoking-related craving can precipitate smoking in abstinent smokers. There appear to be important gender differences in smoking behavior and response to nicotine.

Objective: This pilot study is designed to increase understanding of the neural circuitry underlying nicotine cue-induced craving and to examine possible gender differences.

Method: Nontreatment-seeking nicotine-dependent individuals (five males & five females) and healthy controls (five males & five females) participated in functional magnetic resonance imaging (fMRI) with the presentation of smoking-related cues. Smoking subjects were asked to be abstinent 12 hours before the scanning session. Subjects were assessed for craving, nicotine withdrawal, and CO levels.

Results: Preliminary data suggest activation in the ACC, NA, & amygdala with cue presentation in smokers, but not in healthy controls.

Conclusion: Given the aforementioned differences in brain activity between smokers and healthy controls, the role of gender in activation patterns will also be explored.

P-2: Potentiation of Cue-Induced Reinstatement of Cocaine-Seeking in Female Rats by Yohimbine

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Background and Objective: Clinical research suggests that gender differences exist in cocaine dependence. Similarly, female rats exhibit higher responding during cocaine self-administration and enhanced cocaine-primed reinstatement of drug-seeking. However, limited data exist regarding sex differences in reinstatement following exposure to stress or drug-associated cues, two factors that trigger drug craving and relapse in abstinent cocaine users. Thus, we examined the impact of the anxiogenic a2-noradrenergic receptor antagonist, yohimbine, on reinstatement of cocaine-seeking in rats either in the presence or absence of cocaine-associated cues.

Method: Rats lever-pressed for intravenous cocaine paired with the presentation of a light+tone stimulus for 10 days. Responding was then extinguished in the absence of cocaine or cues. Thirty minutes prior to reinstatement of cocaine-seeking either in the presence or absence of the cocaine-paired stimulus, rats received an injection of yohimbine (0, 1.25 or 2.5 mg/kg).

Results: Yohimbine alone resulted in reinstatement of cocaine-seeking behavior, an effect that was significantly greater in female rats. While cues alone produced comparable cocaine-seeking in both males and females, yohimbine pretreatment in combination with the cues resulted in a supra-additive effect in both groups, with females demonstrating greater yohimbine+cues reinstatement.

Conclusion: While there were no sex differences in response to drug-paired cues, exposure to a stressor alone, or in combination with cocaine-associated cues, resulted in greater reinstatement in female rats. Overall, these results suggest that stress enhances the saliency of drug-associated cues and that the impact of stress activation on drug-paired stimuli may potentiate relapse risk in abstinent cocaine users, particularly females.

P-3: PFIQ Scores Improve after Prolapse Surgery in Women With Depressive Symptoms but Remain Higher than in Women Without Depressive Symptoms

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Background: Little is known about depressive symptoms in women with pelvic organ prolapse (POP).

Objective: To compare pelvic floor-related QOL scores following reconstructive surgery in women with and without depressive symptoms at baseline.

Method: This is an IRB-approved prospective cohort study of 75 women with stage II POP planning surgery designed to assess impact of POP on body image. Subjects were enrolled from a urogynecology practice and completed self-administered measures at baseline and 6 months postoperatively. Measures included the Pelvic Floor Distress Inventory (PFDI), Pelvic Floor Impact Questionnaire (PFIQ), and Patient Health Questionnaire-9 (PHQ-9). PHQ-9 is a validated measure of depression severity. Total scores of =10 correlate with moderate to severe depressive symptoms. Mean values and 95% confidence intervals were determined for the PFDI, PFIQ, and change in scores.

Results: Complete data were available for 58 women. Subjects had mean age 60 ± 8 years, mean BMI 28 ± 5 kg/m2, were predominantly Caucasian (96%) and postmenopausal (82%); a majority had stage III prolapse (83%). At baseline, 23% had moderate to severe depressive symptoms, 77% had none to minimal symptoms. Women with depressive symptoms had higher PFIQ scores compared to women without symptoms at baseline. Women with depressive symptoms had elevated PFIQ compared to women without depressive symptoms.

Conclusion: Pelvic floor disorders appear to have a greater impact on women with depressive symptoms as measured by PFIQ before and after surgery. The relationship between depression, quality of life, and pelvic floor symptoms needs further study to understand the true impact of POP on women.

P-4: Feasibility of a School-Based Coping Intervention for Latino Adolescent Girls

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Background: Latino girls (Latinas) experience higher rates of depression and suicidal ideation than other girls their age and Latino boys. Latina adolescents may benefit from preventive interventions that improve their ability to respond to and cope with life stressors. A coping intervention grounded in the knowledge about healthy youth development was developed for Latina adolescents.

Objective: To evaluate the feasibility and acceptability of a school-based coping intervention for Latina adolescents.

Method: Latina adolescents, 15–21 years old, were recruited from two schools to participate in a 14-week coping intervention. Participants met weekly for a 2-hour program, facilitated by two bilingual staff, consisting of dialogue, exercise, and skills-building. To assess feasibility and acceptability, weekly participation and attendance and post-intervention focus group data were analyzed.

Results: Twenty-one Latina adolescents were successfully recruited. The fall semester intervention (n=10) occurred during school and had a 72% attendance rate; the spring semester intervention (n=11) was held after school and had an 84% attendance rate. Nine of the 21 (42%) participants attended all sessions. Three (14%) attended fewer than half of the sessions and unofficially dropped out. Three participants had limited involvement due to deportation issues involving themselves or a family member. Focus group data demonstrate participant acceptability, "I liked the discussions" and skills gained, "like coping skills to control stress. So when you learn ways to lessen your stress, then you learn to make your life a little easier."

Conclusion: The intervention appears feasible and acceptable. A randomized controlled trial is warranted to examine intervention effectiveness.

P-5: Postpartum Mental Health After Hurricane Katrina

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Background: Natural disaster is often a cause of psychopathology and women are more vulnerable to posttraumatic stress disorder (PTSD) and depression. Postpartum depression is also common. However, no research has addressed postpartum women's mental health after a natural disaster.

Objective: To examine the prevalence and correlates of depression and PTSD among postpartum women affected by Hurricane Katrina.

Method: Two hundred eighty-nine (289) New Orleans and Baton Rouge women were interviewed at 8 weeks postpartum, and 214 at 1 year. PTSD was assessed using the Post-Traumatic Stress Checklist (PCL) and depression using the Edinburgh Depression Scale. Women were asked about their experience with the hurricane with several questions addressing threat, illness, loss, and damage. Chi-square tests and log-binomial/Poisson models were used to calculate associations and relative risks (RR) for hurricane experience and demographics.

Results: Nineteen percent (19%) of women met the criteria for depression and 13% for PTSD. Feeling that one's life was in danger during the storm was strongly associated with depression and PTSD, as were having a family member have an illness or injury, walking through floodwater, and severe impact on property. Overall, two or more experiences of the storm were associated with an increased risk for both depression (RR 1.71, 1.05–2.78) and PTSD (RR 3.49, 1.71–7.12).

Conclusion: Postpartum women who severely experience natural disaster are at increased risk for mental health problems, but overall rates of depression and PTSD are not higher than for the general population.

P-6: Cognitive-Behavioral Therapy for Physical and Emotional Disturbances in Adolescents with Polycystic Ovary Syndrome: A Pilot Study

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Background: Polycystic Ovary Syndrome (PCOS) is the most common endocrinopathy affecting women in the reproductive group, with prevalence rates of 5–12%. Hormonal imbalances in PCOS induce oligoovulation, which is associated with irregular menstruation, hirsutism, and acne. The numerous devastating clinical symptoms of PCOS and associated comorbidities place adolescents with this disorder at an increased risk for physical (obesity) and emotional (depression) disturbances.

Objective: To evaluate the feasibility and effectiveness of an enhanced cognitive-behavioral therapy, Primary and Secondary Control Enhancement Training (PASCET-PI-2), for obesity and depression in adolescents with PCOS.

Method: In an open trial, 12 adolescents (12–18 years, English-speaking, 58% Caucasian, 25% African American) with PCOS, obesity, and depression underwent 8 weekly sessions and 3 family-based sessions of CBT enhanced by lifestyle goals (nutrition and exercise), physical illness narrative (meaning of having PCOS), and family psychoeducation (family functioning).

Results: Weight on calibrated SECA scales showed a significant decrease across the eight sessions from an average of 104 kg (SD=26) to an average of 93 kg (SD=18), $t(11) = 6.6$, $p<.05$. Depressive symptoms on the Children's Depression Inventory significantly decreased from a mean of 17 (SD=3) to a mean of 9.6 (SD=2), $t(11)=16.8$, $p<.01$.

Conclusion: A manual-based CBT approach to treat depression in adolescents with PCOS and obesity appears promising. This investigation utilizes a novel paradigm that incorporates ecological momentary assessment (EMA—wearable monitors that document energy and calorie expenditure and frequent mood-monitoring phone calls) that addresses the shared psychological, behavioral, and biological pathways for physically ill youth.

P-7: The Gender Specification and Cultural Sensitivity of Depression Research With Black Americans: A Multidimensional Model

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Background: Gender differences in depressive disorders are influenced by gender roles and response styles to depressed mood. Yet, a comprehensive understanding of (1) the differences influenced by the intersection of gender, ethnicity,

and culture and (2) the epidemiology, etiology, and risk factors for depressive mood is still needed. For instance, prevalence rates of depressive disorders among black Americans are not clear. While being a woman increases risk for depression, being black does not. Data suggest that black women do not experience depression at higher rates than white women, but they experience depression more often than black men.

Objective: This research (1) highlights findings from an aggregation of scientific knowledge on the influence of gender, ethnicity, and culture on depression in black Americans and (2) presents a multidimensional model of gender specification and cultural sensitivity of depression research on black Americans.

Method: Our objectives were achieved by synthesizing the available research on depressive mood in black Americans and testing the applicability of a multidimensional framework for guiding this research.

Results: Compared to whites, black men and women report greater psychiatric comorbidity, increased severity of somatic symptoms, greater life stress, and differences in perceived physical functioning and health beliefs, which directly influence the presentation of depressive mood.

Conclusion: Before successful mental health interventions can be considered for black Americans and efforts made toward prevention, the development of culturally sensitive and gender-specific programs that achieve optimal mental health are needed.

P-8: Developmental and Situational Crises of Late Adolescence/Early Adulthood in Military Couples With Life-Threatening Fetal Anomalies

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Background: Diagnosis of a life-threatening fetal anomaly constitutes a crisis for pregnant women and their partners who face a difficult decision whether to continue pregnancy. Younger couples face this diagnosis and decisions drawing on limited life experience. Young military couples may be particularly vulnerable to distress in this major adult crisis while still mediating the developmental tasks of late adolescence and early adulthood.

Objective: The purpose of this research is to describe young military couples' decisionmaking and the aftermath in this situational crisis in the context of limited adult development.

Method: Data for this case-intensive ethnography were collected through longitudinal narrative interviews and photography of pregnancy and infant memorabilia. Data from three military couples in the larger study, ages 19–21, were purposefully selected for directed content analysis, framed by extant developmental and situational crisis theories.

Results: In context of early marriage, unplanned pregnancy, separation from family, and deployment or the threat of deployment, couples faced this crisis with little preparation to manage its complexities. Participants described their isolation, shock, and despair; later reactions included anger, hopefulness, and creating meaning of the life of the fetus/baby. Wives continuing pregnancy established elaborate memorials; the couple electing termination wanted little information. Husbands focused on wives' emotional well-being but admitted little understanding; wives described a profound sense of failure and guilt.

Conclusion: When planning and providing care and support to young military couples, healthcare providers should consider the particular complexities of their lives and limited adult development.

P-9: Physical Activity, Menopause, and Quality of Life: The Role of Affect and Self-Worth Across Time

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Background: Physical activity has been shown to enhance quality of life; however, few investigations of these effects exist in women undergoing the menopausal transition.

Objective: The present study examined the long-term effects of physical activity on menopause-related quality of life (QOL) and tested the mediating effects of physical self-worth (i.e., self-esteem specific to the physical domain) and positive affect in this relationship.

Method: Middle-aged women (N = 164, M age = 49.9, SD = 3.6) previously enrolled in a 4-month randomized controlled trial involving walking, yoga, and a control group completed a followup mail-in survey 2 years following the end of the trial. The survey included a battery of psychological and physical activity measures, including measures of menopausal symptoms and menopause-related quality of life. Longitudinal linear panel analysis was conducted within the covariance modeling framework.

Results: At the end of the trial, physical activity and menopausal symptoms were related to physical self-worth and positive affect, and in turn, greater levels of physical self-worth and positive affect were associated with higher levels of menopause-related QOL. Analyses indicated that changes in physical activity and menopausal symptoms over the 2-year period were related to increases in physical self-worth and for symptoms also to positive affect; both physical self-worth and affect directly influenced changes in QOL.

Conclusion: The findings support the position that physical activity effects on QOL are in part mediated by intermediate psychological outcomes and that physical activity can have long-term benefits for women undergoing the menopausal transition.

P-10: Sex Differences in Depression: Roles for Gonadol Hormones and the Developing Hippocampus

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Background and Objective: Women are twice as likely as men to have major depression. Evidence suggests that gonadol hormones play a role in the gender difference of major depression. However, mechanisms of hormonal effects in depression remain unclear. The hippocampus is an effector organ for gonadol hormones during development because both estradiol and testosterone and their receptors are present in perinatal stages. The hippocampus is also a key structure in the pathology of depression. We want to know whether the effects of gonadol hormones on perinatal hippocampal development play a role in depression that develops later in life.

Method: Rat pups were treated with hormones (estradiol, testosterone, dihydrotestosterone (DHT), flutamide, or vehicle) on postnatal day (PND) 0 and 1, and with 5-bromo-2′-deoxyuridine-5′-monophosphate (BrdU) on PND 1, 2, 3 and 4, respectively. Newly produced cells were labeled with BrdU incorroperation; glial cells were identified with antibody against glial fibrillary acidic protein (GFAP). Newly produced glial cells were double-labeled with antibodies against BrdU and GFAP.

Results: (1) Male neonates have significantly more BrdU+ cells than females in the CA1 and dentate gyrus (DG) regions of the hippocampus. Both estradiol- and androgens (testosterone and DHT)-treated females have significantly more BrdU+ cells than vehicle-treated females have in the hippocampus. (2) Male neonates have more GFAP+ cells in the CA1 region than females have; whereas estradiol-treated and testosterone-treated, but not DHT-treated, female neonates, mimicking male neonates, have more GFAP+ cells.

Conclusion: Both estrogen and androgens promote cell genesis in the developing hippocampus, and the estrogen but not androgen may promote gliogenesis.

P-11: An Understanding of the Sex Differences Among Preteen Adolescents at High Risk of HIV and Substance Abuse

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Background: This team showed that preteen girls may use condoms less than male peers. The objective of this study was to determine if there were other sex-based differences between youth at risk of HIV.

Method: We evaluated racially diverse youth from low-income locations in Northern California who were concurrently enrolled in an HIV-prevention project. Detailed surveys were used to collect data on household information; youth described behavior involving sex, drug use, and HIV knowledge.

Results: Preteen girls (n=113) showed more self-efficacy for increased condom use, decreases in alcohol use with sex, and resistance to sexual pressure compared with preteen boys (n=114) in a sexual risk assessment scale (9.7 vs. 11.1, $p<0.05$); girls and boys have the same perception of individual HIV risk score (2.3 vs. 2.4, p= ns), and HIV knowledge scores were the same in both groups. (p= ns). In models predicting sexual behavior, boys consistently had more sexual activity than girls, even correcting for age, religious conviction, living condition, and drug use AOR: 1.79 (CI; 95% 1.47–2.18). After adjusting for age, religious belief, sexual activity experience, HIV knowledge, and living situation, preteen boys and girls used condoms the same amount, AOR:0.91 (CI 95% .66–1.27).

Conclusion: Preteen girls in northern California have more confidence in their real world ability to limit high-risk behavior compared to boys, but tend to have very similar risk behavior. These findings suggest an increased need to focus on behavior rather than intent to decrease HIV acquisition in youth.

P-12: Acceptance of Human Papillomavirus (HPV) Vaccination by Low-Income, Minority Parents

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Background: Cervical cancer is more common among low-income and minority women. HPV vaccination has the potential to reduce healthcare disparities if widely utilized.

Objective: To characterize attitudes toward HPV vaccination in low-income, minority parents.

Method: Parents of vaccine-eligible girls were interviewed before preventive health visits. Interviews assessed knowledge of vaccine-preventable diseases, attitudes toward HPV vaccination, and intention to vaccinate. Actual vaccination rates were determined by chart review.

Results: Seventy-six (76) parents (93% female) participated: 32 African-American, 21 Latino, 21 Caucasian, and 2 other races. Mean age was 43, and mean education level was 13 years. Eighty-two percent (82%) expressed a religious affiliation; 50% were foreign-born, and 65% spoke English as their primary language. Parents answered 49–66% of questions correctly about vaccine-preventable diseases. Knowledge scores were similar across ethnic groups, and were similar for HPV and other vaccine-preventable diseases: varicella, Hepatitis B, and pertussis. Qualitative data indicated that parents believed teenagers experimented sexually against parental advice and saw HPV vaccination as a way of protecting their children against sexually transmitted diseases and cancer. However, they were concerned that vaccination could invite earlier or unsafe sexual activity or have unknown side effects. Ninety-one percent (91%) of parents supported HPV vaccination for their daughters. Acceptance did not vary by ethnicity. Reasons for declining included wanting more information, feeling vaccination was unnecessary, religion, and side effects. However, only 70% of girls received vaccination. Physicians failed to offer vaccination to the remaining girls.

Conclusion: Low-income and minority parents have high rates of HPV vaccine acceptance and physicians may not be meeting parental demands.

P-13: Type-Specific Concordance Among Monogamous Couples in Whom the Woman Had a Recently Detected, Incident HPV Type

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Background: HPV concordance between couples is low despite sexual transmission.

Objective: To examine concordance between monogamous couples in which the woman had a recent, incident HPV type.

Method: Women participating in a longitudinal study being tested every 4 months for HPV were recruited for participation with their monogamous male partner if they had an incident, cervical HPV type at their most recent visit. Sites tested were: oral, palm, and anogenital area. HPV-DNA PCR used PGMY09/11 primers (Roche Molecular Systems).

Results: Twenty-five (25) couples were enrolled; 94% of samples were adequate. Five couples had only one partner with HPV. In three couples, neither partner had HPV. HPV was detected in both partners in 17 couples. Of these, four couples had no type-specific concordance. Thirteen had type-specific concordance. All 13 had type-specific concordance at anogenital sites, three had type-specific palmar concordance, one had oral concordance. Four had type-specific concordance for all types detected in the anogenital area. Nine had type-specific discordance in addition to type-specific concordance in the anogenital area. Two couples in whom a type was detected in the anogenital area of one partner but not the other had the type detected in the mouth or hand of the anogenital-negative partner.

Conclusion: Type-specific HPV concordance in monogamous couples is common in the anogenital area, specifically

in women with recent, incident HPV detected. Although the palm and mouth were uncommon sources for infections, when anogenital type-specific discordance occurs, the discordant type may be found in nongenital areas of the anogenital negative partner.

P-14: HPV Risk Association in Urban Populations

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Background: HPV risk profiling from published HPV prevalence studies was used as the basis of the risk-association tool.

Objective: To identify HPV-associated risk factors.

Method: Design—Cross-sectional convenience sample of 200 adult women. Setting—Urban University of Maryland Family Medicine clinic (UMFMC). Patients—IRB assurances received. Adult women age 18 and over, English literacy. Instrument—A multi-item scale to identify HPV-associated risk factors including two demographic items, one item regarding HPV status by history, five items on medical and reproductive history, five items on sexual history, and three social history items. The tool was computerized and administered using tablet PCs.

Results: Two hundred (200) women completed the survey. There were 47% women age >30; 10.6% were positive for HPV by history, 16.2% had prior abnormal Pap smears, and 39.9% had prior sexually transmitted disease. Sexual debut was <16 years in 43.4% and 21.2% had casual sexual partners. HPV-positive women had significant association with abnormal Pap smear (p-value 0.0001), STD (p-value 0.0018), and with illicit drug use (p-value 0.0002).

Conclusion: HPV infection by history is associated with abnormal Pap smears, prior STD, and drug use. This tool has the potential for use in risk stratification, linkage to health education, and as an entry point into HPV vaccination, HPV screening, and to clinical trials in HPV.

P-15: Gender-Specific Differences in the HIV Release Mechanisms

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Background: Women who transmit HIV have been reported to have four times higher viral loads than those who do not. In addition, women progress to AIDS at lower viral loads and higher CD4 counts than do men, a characteristic that has significant implications for treatment of HIV-infected women. The mechanisms underlying these differences in HIV viral loads in men vs. women are not understood.

Objective: The goal of this study was to test whether differences in the cellular mechanisms that influence HIV release account for the disparity in viral loads between the genders. We have recently identified a cellular protein, calcium-modulating cyclophilin ligand (CAML) that restricts HIV release from human cells. We tested endogenous levels of CAML in primary lymphocytes derived from age group-matched women and men.

Method: The levels of expression of CAML were assayed by Western blotting and real-time PCR.

Results: The results from Western blotting analysis indicate significantly lower amounts (3–4 fold) cellular CAML in younger women belonging to the 20–30 years age group compared to that of males. Further, the levels of CAML protein in cells obtained from women also correlated with the reduced CAML mRNA (CAMLN relative to Male ~0.10 –0.25) as indicated by real-time PCR. In contrast, we did not note gender-specific differences in the cellular levels of CAML in the subjects belonging to the 45–50 years age group.

Conclusion: These data suggest that CAML levels dictate the differences in viral loads, especially in the younger women, and thereby might influence the dynamics of HIV transmission.

P-16: A Teen Clinic Intervention To Reduce Partner Violence Among Adolescent Females: A Feasibility Study

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Background and Objective: One in five female high school students report experiencing physical and/or sexual violence from a dating partner, and these experiences are highly correlated with poor health outcomes. Barriers to case identification in the adolescent clinical setting include limited adolescent care-seeking for partner violence, healthcare provider discomfort, and lack of evidence-based interventions to reduce adolescent partner violence. Our objective was to obtain information from providers and school-based clinic patients regarding a possible intervention to identify and address adolescent partner violence in school health centers.

Method: Qualitative interviews were conducted in a school-based health center with nurse practitioners (N=3) (trained in the dating violence intervention) and patients (ages 14–17 years, N=10) about the feasibility and potential utility of a clinic-based intervention adapted for use in teen clinics. Interviews were transcribed, coded, and analyzed utilizing a content-analysis approach. Specific attention was paid to identifying themes related to implementing the intervention, including concerns about effects on clinic flow (providers) as well as confidentiality (patients).

Results: Preliminary findings from the nurse practitioner interviews indicate a willingness to utilize the intervention and concerns about time pressures and lack of resources to assist patients. Patients were interested in receiving additional educational materials and discussing partner violence in this clinical setting, but expressed specific concerns about disclosure and confidentiality.

Conclusion: A brief clinic-based intervention adapted for teen clinics appears to be acceptable for nurse practitioners and patients. Whether this intervention is effective in changing adolescent knowledge and behaviors regarding partner violence requires further testing.

P-17: A Conceptual Framework for Contraceptive Decisions Based on Decision Support

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Background: The majority of unintended pregnancies in the United States occur despite contraceptive use, which is a function of contraceptive choices; less effective methods are commonly used but highly effective methods are rarely so.

Improving contraceptive decisions would decrease the unintended pregnancy rate.

Objective: Apply the Ottawa Decisional Support Framework (ODSF) to contraceptive decisions using known factors that influence contraceptive decisions in preparation for a qualitative study.

Method: We reviewed the literature to identify factors that influence contraceptive decisions. We applied the ODSF to these factors to assess the determinants of the decision. ODSF is appropriate for health decisions that are value-laden and do not have a clear best choice.

Results: The literature review for contraceptive preferences, attitudes, and use revealed 17 studies of adult U.S. women published from 1970 to 2008. Characteristics of women, methods, and healthcare providers were identified as factors related to contraceptive choice or use. The characteristics mapped to three of four determinants of decisions: resources to make a decision (personal and external support), characteristics (client and practitioner), and perception of decision. Two important themes within perception of decision were not explored in any study: conflict and stage of decision making. No factors mapped to the fourth, perception of others.

Conclusion: Optimizing contraceptive decisionmaking is crucial to reducing unintended pregnancies. The ODSF can inform the development of decision support tools to optimize contraceptive decisions. Future work will explore unexamined themes related to perceptions of others and perceptions of the decision to assess the determinants of the contraceptive decision.

P-18: Over-Expression of Secreted Frizzled-Related Protein 1 Inhibits Bone Formation and Attenuates PTH Bone Anabolic Effects

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Background and Objective: Secreted frizzled-related protein 1 (sFRP1) is a soluble antagonist of the Wnt signaling pathway. In this study, we investigated how over-expression of sFRP1 (sFRP1-Tg) would affect bone formation and its interaction with PTH treatment.

Method: Three-month-old WT or sFRP1-Tg male and female mice (n=7–12/group) were treated with PTH (1–34) (40μg/d, 5x/wk) or Vehicle for 2 weeks. We monitored bone architectural and bone turnover changes by microCT, bone markers, and histomorphometry. Osteoblastic and osteoclast maturation and function were accessed by primary bone marrow stromal cell and osteoclast cultures.

Results: Males, but not females, had lower trabecular bone mass (-32%). Genes associated with osteoblast maturation (Runx2, SP7) and function (Bgalp), serum osteocalcin, mineral apposition rate (MAR), and bone formation rate (BFR) were significantly decreased in sFRP1-Tg mice from both genders. Bone resorption, measured by serum CTX-1, and osteoclast surface were similar between sFRP1-Tg and WT in vivo but was higher in sFRP1-Tg in vitro. Human PTH (1–34) treatment for 2 weeks increased trabecular bone volume (female, +156% and male +319%) in WT mice as compared to 84% in female and 103% in male sFRP1-Tg mice ($p < 0.05$ for PTH x genotype). Percentage increases in MAR and BFR were lower in PTH-treated sFRP1-Tg mice than the PTH-treated WT mice.

Conclusion: Over-expression of sFRP1 inhibited osteoblast maturation and function and attenuated PTHs anabolic action on bone. Gender differences in bone phenotype of the sFRP1-Tg animal and gender-specific response to PTH are being investigated.

P-19: Genetic Variants in the Transforming Growth Factor-β (TGF-β) Signaling Axis in Patients with Scleroderma

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Background: Scleroderma (SSc) is a complex, multigenic, fibrotic disease. Transforming Growth Factor-β (TGF-β) is thought to activate tissue fibroblasts causing fibrosis. The aim of this study was to identify the associations between genetic polymorphisms of the TGF-β signaling pathway and SSc.

Objective: We investigated the role of two common and functionally relevant variants of the TGFB1 and TGFBR1 genes, in a clinically well-characterized cohort of SSc patients and healthy controls. We tested the hypothesis that the hypomorphic TGFBR1*6A allele is associated with a decreased risk of developing SSc and that the TGFB1 T29C single nucleotide polymorphism (SNP) that results in higher circulating levels of TGF-β is associated with an increased risk of developing progressive SSc.

Method: DNA from 80 consecutive patients with SSc who fulfilled ACR criteria for diagnosis and 160 healthy controls was genotyped. A case-control analysis was performed using conditional logistic regression to estimate age-, gender-, race-, and smoking status-adjusted relative risk.

Results: A 6A/6A or 9A/6A genotype was associated with an adjusted odds ratio for developing SSc of 0.651 (95% CI 0.270, 1.570). A CC/TC genotype was associated with an adjusted odds ratio of 0.624 (95% CI 0.323, 1.204).

Conclusion: Preliminary results suggest a trend toward an association for lower risk of SSc with the TGFBR1 6A/6A or 6A/9A genotype, but the result is not statistically significant (p=0.339). Unexpectedly, the CC/TC genotype for the TGFB1 ligand resulted in a decreased risk for SSc, though the result was not statistically significant (p=0.160).

P-20: Genetic Linkage Localizes the Adolescent Idiopathic Scoliosis and Pectus Excavatum Gene to Chromosome 18q

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Background: Adolescent idiopathic scoliosis (AIS) and pectus excavatum (PE) are common musculoskeletal conditions known to have a genetic component, though few causative genes have been identified.

Objective: To map the disease-causing locus in a large Caucasian family in which AIS and PE co-segregate.

Method: Clinical examinations were performed on the proband, who underwent posterior spinal fusion, and 12 additional affected family members. To map the gene causing AIS and PE, a genome-wide linkage analysis was performed with the Affymetrix Mapping 10K array on 13 affected and

10 unaffected family members. Candidate genes were sequenced.

Results: AIS was present in 13 female family members and PE was present in 3 males and 1 female. Genome-wide linkage analysis resulted in a linkage peak on chromosome 18q with a maximum parametric multipoint logarithm of the odds (LOD) score of 3.86. Recombinants delineated the critical genetic region to an interval of 6.4 cM region [corresponding to 7.06 Mb region (hg18: chr18:26342508–34395660)]. The chromosome 18q linkage region contains more than 30 genes. Resequencing of the coding regions of 21 candidate genes in the region did not reveal any causative mutation.

Conclusion: Linkage analysis of this large family suggests that an AIS and PE susceptibility gene resides on chromosome 18q. PE is common in families with AIS, and consideration of family members with PE as affected may increase the power of AIS genetic linkage studies.

P-21: Doublecortin Regulates Dendritogenesis Through Interaction With Kinesin1a

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Background: Mental retardation is a disorder that has a greater prevalence in males compared to females. How mutations in X-linked genes result in mental retardation is not known. Work in animal models has revealed a role for doublecortin, a gene that causes X-linked mental retardation and epilepsy, in neuronal development.

Objective: To understand the cell biology of doublecortin family proteins with respect to disease pathogenesis.

Method: We used dissociated hippocampal cultures from Dcx/Dclk mutant embryos to characterize the different stages of neuronal development with immunocytochemistry and confocal imaging. We have used protein chemistry methods to demonstrate an interaction with kinesin1a and RNAi of kinesin 1a to phenocopy Dcx/Dclk effects.

Results: Characterization of Dcx-/y;Dclk-/- neurons in dissociated cultures demonstrates a novel defect of dendritogenesis. There is a delay in the formation of the primary dendrite. Likewise, the Golgi, which is associated with dendritic morphology, does not track up the dendrite in the mutant neurons. We show an interaction of Dcx with kinesin1a and RNAi of kinesin1a phenocopies Dcx/Dclk knockdown with respect to the dendritic and Golgi morphology.

Conclusion: These results point to a novel role of doublecortin, a cytoskeletal protein, in the regulation of the Golgi secretory apparatus during neuronal development, leading to abnormal dendrites in the absence of functional Dcx/Dclk. The effects of Dcx are likely mediated through its interaction with the motor protein, kinesin 1a. Dendritic abnormalities are associated with mental retardation and these may be the basis of cognitive dysfunction in DCX patients, as well.

P-22: The Anti-Apoptotic Kinase Akt2 Is a Critical Mediator of Glut1 Sensitive Neuronal Apoptosis

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Background: Glucose is the primary energy substrate for eukaryotic cells and the sole substrate for the brain. There is increasing evidence that glucose serves an additional role in the regulation of cellular functions including viability. Studies from our laboratory established zebrafish as a tractable system for defining the cellular and molecular mechanisms affected by impaired glucose metabolism. Inhibiting the expression of the ubiquitously expressed glucose transporter, Glut1, results in severe embryonic neurodegeneration caused by increased neuronal apoptosis.

Objective: The objective of this study was to define downstream components of the observed Glut1 sensitive apoptotic pathway. Specifically, we aim to define the role of Akt2 as a possible mediator.

Method: The method of targeted knockdown of Akt2 was employed utilizing specialized anti-sense oligonucleotides, morpholinos.

Results: Results reveal that impaired expression of Akt2 causes a syndrome similar to that observed by abrogation of Glut1. Akt2 morphants exhibit increased neuronal apoptosis, impaired glucose uptake, and embryonic death by 72 hours-post-fertilization. Inhibiting the expression of the anti-apoptotic protein, Bad, resulted in the inhibition of apoptosis and rescue of the Akt2 morphant embryos. Intriguingly, we discovered that the Akt2 morphant embryos could also be rescued by over-expression of Glut1.

Conclusion: The conclusions from this study are that Akt2 is integrally involved in the Glut1 sensitive apoptotic pathway described previously. We hypothesize that Akt2 is affecting glucose metabolism by decreasing expression of Glut1 resulting in decreased glucose availability, which in turn affects Akt2, whose activity is known to be dependent on available glucose, culminating in the observed neurodegenerative phenotype.

P-23: Uncontrolled Asthma During Pregnancy Is Associated With an Exaggerated Th1:Th2 Cytokine Phenotype

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Background: Asthma is a chronic inflammatory disorder of the lower airways that is associated with a Type-2 helper T-cell (Th2) cytokine environment. Uncontrolled asthma during pregnancy has several adverse effects on the mother and fetus. Identification of women who will experience uncontrolled asthma in pregnancy is difficult, but characterizing the altered cytokine environment of pregnancy may help identify those at risk.

Objective: To determine if an exaggerated Th2 cytokine environment characteristic of pregnancy will be associated with uncontrolled asthma in pregnancy.

Method: Sixteen subjects (11 controls, 5 asthmatics) followed during the 2nd and 3rd trimesters of pregnancy, completed Asthma Control TestsTM, spirometry, exhaled nitric oxide, and blood draws at study visits. Peripheral blood mononuclear cells were stimulated with phytohemagglutinin and cell culture supernatants were assayed for cytokines using a Luminex100 analyzer. Descriptive statistics and t-tests were performed.

Results: Uncontrolled asthma was associated with a more pronounced Th1 phenotype compared to controlled asthma as assessed by the average IFN-γ:IL-4 ratio of each group (45.84 vs. 9.49, respectively; $p=0.03$). Similar trends were found for other Th1:Th2 cytokine ratios, such as IFN-γ:IL-5 (1092.47 vs. 267.04, $p=0.15$) and IFN-γ:IL-13 (11.69 vs. 2.27, $p=0.11$). Compared to healthy controls, uncontrolled asth-

matics also demonstrated lower IFN-γ:IL-10 ratios (1.30 vs. 0.72, p=0.03).

Conclusion: Uncontrolled asthma was associated with a more pronounced Th1, and not Th2, cytokine environment compared to controlled asthma. Further studies using these cytokine ratios earlier in pregnancy to predict which asthmatics will worsen should be performed.

P-24: The Cell Surface Phenotype of Uterine Natural Killer Cells: Markers of uNK Activation

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Background: Recently a subset of natural killer (NK) cells was identified based on the cell surface phenotype B220+NK1.1+CD11c+CD11b+CD27+. This NK cell population produces greater amounts of IFN-γ than conventional NK cells. Phenotypically, these cells resemble human uterine natural killer (uNK) cells; however, the physiologic role of this murine cell population is unknown.

Objective: Determine whether murine uNK cells belong to the B220+NK1.1+CD11c+CD11b+CD27+ subset of NK cells. Elucidate whether peripheral NK cells of the B220+NK1.1+CD11c+CD11b+CD27+ subset are specifically recruited to the uterus during gestation and/or whether this cell surface phenotype is indicative of uNK cell activation status.

Method: Uteri were isolated from virgin mice or pregnant mice at E6.5–10.5. A single cell suspension was generated. The cells were stained with specific antibodies and analyzed by flow cytometry.

Results: The vast majority of uNK cells at E10.5 were B220+NK1.1+CD11c+CD11b+CD27+. uNK cells from virgin mice expressed low levels of B220. However, B220 protein expression increased on a subset of uNK cells from E8.5 through E10.5. This is the time frame in which uNK cells become activated. Moreover, the B220hi population of uNK cells expressed activation markers, including ICOS, whereas uNK cells derived from virgin mice did not.

Conclusion: uNK cells at E10.5 are B220+NK1.1+CD11c+CD11b+CD27+ similar to the recently characterized peripheral NK cell population. We speculate that uNK cell activation is reflected by increased B220 expression. Thus we believe B220hiNK1.1+CD11c+CD11b+CD27+ cells are activated uNK cells. Studies are currently underway to determine whether B220+ NK cells are preferentially recruited to the uterus during pregnancy.

P-25: Nitric Oxide and Vascular Endothelial Growth Factor During Pregnancy in Sickle Cell Disease

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Background: Women with sickle cell disease (SCD) are more likely to deliver small for gestational age (SGA) infants than women without the disorder. Poor placental perfusion and small infant size have long been attributed to sickle erythrocytes. However, patients with SCD are deficient in the vasodilator nitric oxide, NO, which could compromise vasodilation in the placental vascular bed. A potent inducer of NO release is VEGF. Pregnant women with SCD have high plasma levels of a VEGF antagonist, sFLT-1, which has been implicated in SGA infants. Although there may be a relationship between NO, VEGF, and sFLT-1 in SCD, no study has sought to explore this association or its impact on SGA infant status.

Objective: To interrogate levels of NO, free VEGF, and sFLT-1 during pregnancy in SCD and to explore the relationship between NO, sFLT-1, and SGA infant status.

Method: We performed an analysis of previously collected plasma/serum samples obtained through the Pregnancy, Infection, and Nutrition study cohort. Levels of free VEGF and sFLT-1 were quantified by ELISA. NO was quantified via its metabolite NOx using a modified Griess method.

Results: Free VEGF and NO were significantly lower in pregnant women with SCD than in matched pregnant controls. We also found a significant association between NOx and sFLT-1 levels. Pregnant women with SCD who delivered an SGA infant also had significantly lower levels of NOx than those women who did not.

Conclusion: These results suggest that impaired release NO may play a role in SGA infant status in SCD pregnancies.

P-26: Human Cumulus Cells in Culture: Tools To Evaluate Oocyte Quality?

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Background and Objective: Within ovarian follicles, cumulus granulosa cells surround the oocyte and play crucial roles during oocyte growth, development, and maturation. Cumulus cells, therefore, may serve as indicators of oocyte quality during assisted reproductive technology (ART). However, little is known about human cumulus cell function or regulation. Here, we examine the production of estrogen and progestins by cumulus cells in culture, their response to pituitary gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and their protein profile(s).

Method: Cultured cumulus cells were isolated from oocytes collected from women undergoing ART. Progesterone and estradiol were measured by EIA following treatment with forskolin, FSH, or human chorionic gonadotropin (hCG). Aromatase activity, necessary for estrogen biosynthesis, was determined by tritiated water assay. mRNA accumulation was quantitated by real-time PCR. Protein profiles of cumulus cell extracts were examined by iTRAQ analysis.

Results: Estradiol biosynthesis, P450 aromatase activity, and associated CYP19 mRNA accumulation were elevated by forskolin, hCG, or FSH treatment. P450 cholesterol side-chain cleavage (CYP11A1) mRNA and progesterone biosynthesis were similarly induced by hCG or FSH. Proteomic analyses revealed a subset of proteins with altered abundance (increased or decreased) in hCG-treated cells, as compared to nonstimulated cells.

Conclusion: Cultured cumulus cells are steroidogenic cells that respond to gonadotropins with increases in progesterone and estradiol biosynthesis and associated mRNA expression. Further evaluation of cumulus cell steroidogenesis and protein profiles from individual oocytes may reveal cumulus-specific function(s) during follicular development and identify markers of oocyte competence to improve outcomes for women undergoing ART.

P-27: Epigallocatechin-3-Gallate (EGCG) Ameliorates Hyperglycemia-Induced Malformation by Inhibition of Foxo3a Activation

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Background: Maternal hyperglycemia increases risks of congenital malformations. Hyperglycemia-induced oxidative stress is responsible for this teratogenic effect. Hyperglycemia triggers activation of Foxo3a (Forkhead transcription factor 3a), manifested in the reduction of phosphorylated Foxo3a (pFoxo3a) at threonine 32, which leads to Foxo3a nuclear translocation. Foxo3a mediates oxidative stress signaling and may be involved in hyperglycemia-induced malformations. EGCG, a natural antioxidant, is a purified green tea compound that inhibits oxidative stress signaling. Thus, we propose that EGCG prevents hyperglycemia-induced malformation via inhibition of oxidative stress signaling.

Objective: In this study, we examined the effect of EGCG on hyperglycemia-induced malformation and Foxo3a activation.

Method: Embryonic day 9 rat conceptuses were cultured under euglycemic (150 mg/dl) and hyperglycemic (300 mg/dl glucose) conditions with or without 1 or 10 μM EGCG. After 48 h, embryos were dissected from yolk sacs and morphologically examined for malformations. Levels of pFoxo3a and pAkt, a kinase that specifically inhibits Foxo3a activation, were determined in embryonic lysates by Western blotting.

Results: At concentrations of 1 μM or 10 μM, EGCG had no teratogenic effect on embryonic development. Both 1 μM and 10 μM EGCG completely prevented hyperglycemia-induced embryonic malformations. While hyperglycemia inactivated Akt by reducing pAkt levels, EGCG reversed the inhibitory effect of hyperglycemia on Akt activation. EGCG prevented hyperglycemia-reduced pFoxo3a levels and thus abolished hyperglycemia-induced Foxo3a activation.

Conclusion: EGCG prevents hyperglycemia-induced malformation in vitro through inhibition of Foxo3a activation. This may have been mediated via the activation of Akt. These findings offer the potential for a possible pharmacological prophylaxis.

P-28: Development of a Novel Three-Dimensional Ovarian Organ Culture To Study Surface Repair as a Mechanism for Ovarian Cancer Formation

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Background: The fewer times a woman ovulates, the lower her risk for developing ovarian cancer. Ovarian cancer is difficult to study due to the lack of models for identifying changes in the ovarian surface epithelium (OSE), the cells responsible for 90% of ovarian cancers.

Objective: We sought to establish that repeated tear and repair of the OSE from ovulation increases the risk of ovarian cancer due to enhanced proliferation and migration of the OSE.

Method: We developed a novel three-dimensional ovarian organ culture using artificially wounded ovaries embedded into alginate gels.

Results: Using an ovarian organ culture, OSE repopulated the outer surface of the wounded tissue in a time-dependent manner. The cells that encapsulated the wounded surface maintained characteristics of normal, healthy OSE cells such as expression of cytokeratin 8, N-cadherin, vimentin, and an absence of E-cadherin. Growth of ovarian organ cultures in medium supplemented with bovine serum albumin increased the proliferation of OSE based on bromodeoxyuridine incorporation while medium supplemented with fetal bovine serum enhanced OSE cell migration. The fastest proliferation rates were measured after wounding on day 2 and slowed as the surface became more highly encapsulated.

Conclusion: Ovarian surface repair can now be studied in vitro using an organ culture model and reveals that the wounding process induces proliferation and migration of the OSE. Because a hallmark of cancer is the process of uncontrolled proliferation and migration of cells, our studies connect the process of wound repair as it relates to ovulation and cancer formation.

P-29: Parity Is Associated With Altered Collagen Subtypes and Inferior Biomechanical Properties in the Primate Vagina

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Background: Vaginal injury at the time of delivery is considered one of the greatest risk factors for developing a pelvic floor disorder later in life.

Objective: The objective of this study was to quantify the extent of injury or incomplete recovery following vaginal delivery by comparing the collagen ratios and uniaxial mechanical properties of the vaginal wall in parous and nulliparous nonhuman Rhesus macaques.

Method: The vaginas of six parous (median vaginal parity of 7) at least 1 year from the most recent delivery and three nulliparous primates were utilized. Fibrillar collagens I, III, and V present in the subepithelium of the midvagina were assessed via quantitative fluorescence microscopy (N=3 in both groups). To measure the mechanical properties of the vagina, a uniaxial tensile test was performed on all specimens. Biochemical and biomechanical data were compared using a Mann-Whitney test with significance set at $p<0.05$.

Results: Parity was associated with a decrease in the ratio of collagen I/III+V in the subepithelium (0.31 ± 0.04 vs. 0.14 ± 0.06, $p<0.05$), primarily due to an increase in collagen III. Correspondingly, the parous group demonstrated a significantly lower tensile strength and strain-energy density, which both measured 2.5 times less that of the nulliparous group ($p< 0.05$).

Conclusion: Parity is associated with altered collagen subtypes and inferior biomechanical properties resulting in a decrease in the ratio of collagen I/III+V as well as a decrease in strength and toughness. These changes may contribute to the progression of pelvic organ prolapse over time.

P-30: Effects of Estrogen on the Biophysical Properties of Hippocampal CA1 Pyramidal Neurons

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Background: For female ovariectomized animals, the longer the time interval between surgery and the initiation of estrogen replacement therapy, the less responsive the neural tissue be-

comes to exogenous estrogen treatment. Estrogen regulates gene expression and neuronal activity in many central neurons.

Objective: To test whether or not the expression profiles of ion channels and receptors that directly bind estrogen are gradually altered following estrogen withdrawal.

Method: Whole-cell current clamp recordings were used to assess the intrinsic membrane excitability of hippocampal CA1 pyramidal neurons from ovariectomized female rats that were deprived of estrogen for either 7 days or 5 months (short- or long-term estrogen deprivation).

Results: Bath application of estrogen significantly increased the excitability of CA1 pyramidal neurons from only short-term, but not long-term, estrogen-deprived rats. Long-term estrogen deprivation significantly reduced the excitability of CA1 pyramidal neurons.

Conclusion: Estrogen is important in maintaining the cellular profile of ion channels and receptors that regulate the excitability of CA1 pyramidal neurons. As the hippocampus is crucial for learning and memory and CA1 pyramidal neurons are its principle output neurons, these results may be related to the intriguing clinical findings that estrogen replacement therapy impedes age-related cognitive decline in women only when initiated near the time of menopause, but not 10 or more years following menopause. Understanding the actions of estrogen on CA1 pyramidal neurons and identifying its targets are pivotal steps toward evaluating current strategies for estrogen replacement therapy and will lead to the design of gender-specific therapeutic interventions to treat cognitive deficits.

P-31: 2-Methoxyestradiol Induces Apoptosis of Pulmonary Microvascular Endothelial Cells: A Potential Therapy for Pulmonary Hypertension

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Background: Primary pulmonary hypertension (PH) is a relatively rare but lethal disorder characterized by poor median survival rates. Current research suggests the culprit lesion in PH comprises highly proliferative vascular endothelial cells that are resistant to apoptosis. A particularly intriguing aspect of this research is the potential for estrogen metabolites with potent growth inhibitory effects to influence this process. 2-Methoxyestradiol (2-ME) is a potent anti-estrogen metabolite that inhibits angiogenesis and promotes apoptosis in multiple cell lines. It is being administered in several phase-II clinical trials in disease states and may represent a potential therapy in PH.

Objective: To evaluate the effects of 2-ME on human pulmonary vascular endothelial cell apoptosis and explore potential mechanisms involved in 2-ME-induced apoptosis.

Method: HMPVC were purchased and maintained in supplemented media. 2-ME was added, and cellular proliferation was assessed by MTT colorimetric assay. In additional experiments 2-ME-induced cellular apoptosis was assessed by flow cytometry. Lastly, RNA was extracted from 2-ME-treated cells, and QPRC for UPR targets was performed.

Conclusion: Treatment of human pulmonary microvascular endothelial cells with 5uM 2-ME at 48 h resulted in decreased cellular proliferation as compared to controls. 2-ME-induced reduction in cell proliferations was not affected by co-incubation with estradiol or SHBG. 2-ME-induced apoptosis of HMPVC in a dose-dependent manner. This treatment was associated with increased expression of key targets in the unfolded protein response. These results suggest that 2-ME-induced apoptosis may involve the endoplasmic reticulum stress response.

P-32: Severe Pulmonary Hypertension Is Associated With an Increased Plasma Ratio of Estrogenic to Antiestrogenic Metabolites

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Background: Severe pulmonary hypertension (PH) is a lethal disorder characterized by marked angiogenesis and endothelial cell proliferation in the microcirculation of the lung. PH affects women disproportionately. The female-male ratio is 3:1, and the gender differences are observed in the idiopathic as well as secondary forms of the disease. These sex-based differences are particularly intriguing given the potential for sex steroids to modulate key pathogenic processes in severe PH. The major estrogen produced in the ovaries is 17-B estradiol (E2). E2 is a potent inducer of endothelial cell proliferation in the lung. E2 can be further detoxified to 2-ME. This metabolite is distinctly anti-estrogenic and induces apoptosis in several cell lines. Inter-individual differences exist in key enzymes required for estrogen detoxification. Such differences may predispose to the development of diseases characterized by angiogenesis such as severe PH.

Objective: To assess for an estrogen metabolite profile that would favor angiogenesis in patients with established severe PH.

Method: Plasma was collected from patients referred for evaluation of PH in our multidisciplinary PH clinic. Quantification of circulating endogenous estrogens was performed via liquid chromatography-tandem mass spectrometry. The ratio of E2 to the anti-estrogen metabolite 2-ME was compared between patients meeting criteria for severe PH and controls.

Results: The ratio of E2 to 2-ME was significantly higher in patients with severe PH as compared to controls. Further study is warranted to evaluate these preliminary associations between estrogen tone and severe PH.

P-33: Cell-Type-Specific Regulation of Transcription by Estrogen

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Background: Estrogen is an important regulator of development and plays a role in the bone, among other tissues. Many of the genes regulated by estrogen in the bone remain unknown, and the mechanism by which estrogen exerts tissue-specific effects remains to be explained.

Objective: To identify osteoblast- and breast-specific genes regulated by estrogen and to understand the mechanism of tissue specificity.

Method: We have compared the global gene expression profile of the MCF7 breast cancer cell line with that of the osteoblast-like cell line U2OS-ERa by expression microarrays, and we compared the ER alpha binding sites in the two cell types by performing chromatin immunoprecipitation (ChIP) on genomic tiling arrays (ChIP-on-chip).

Results: We find that fewer than 10% of the estrogen-regulated genes are common to both cell types. We have validated many of these genes in primary calvarial osteoblasts. ERalpha binding in U20S-ERa cells best correlates with genes up-regulated in U20S-ERa cells, and ERalpha is recruited to multiple enhancers near genes induced by estrogen. Interestingly, while the forkhead factor FoxA1 plays a critical role

in defining the ERa binding sites in MCF7 cells, it is not expressed in U2OS-ERa cells, and forkhead motifs are not enriched in the ERalpha binding sites in these cells. Finally, the ERalpha binding sites are correlated with cell-type-specific epigenetic histone modifications.

Conclusion: These results support a model for the cell-type-specific action of estrogen being driven primarily through specific ERalpha occupancy of epigenetically marked cis-regulatory regions of target genes.

P-34: The Role of ABC Transporter in Export of Sphingosine 1-Phosphate From Breast Cancer Cell

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Background: Sphingosine 1-phosphate (S1P) is an active lipid mediator, which plays critical roles in cancer progression. S1P is produced by only two specific isoenzymes, sphingosine kinase 1 (SphK1) and 2 (SphK2). SphK1 is over-expressed in breast cancer. S1P binds to its specific receptors on the cell surface and exerts its biological effects. However, it is not known how intracellularly produced S1P is exported out of these cells.

Objective: To investigate whether ABC transporter plays a role in S1P export of breast cancer, and to examine whether SphK1 or SphK2 is responsible for the export of S1P.

Method: MCF-7 breast cancer cells were used as a model. SphK1 and SphK2 were over-expressed by transfection of respective plasmid, and knocked down using specific siRNAs. S1P was measured using 3H labeled sphingosine, and mass spectrometer.

Results: Over-expression of SphK1, but not SphK2, increased S1P export, although both similarly increased intracellular levels of S1P. Conversely, down regulation of SphK1, but not SphK2, decreased export of S1P. Estradiol phosphorylated SphK1 immediately after stimulation that resulted in S1P export, which was inhibited by an inhibitor of ABCC1 and ABCG2, but not ABCB1.

Conclusion: This is the first demonstration in which the multidrug resistant transporters, ABCC1 and ABCG2, are involved in estradiol-induced export of S1P. Further, SphK1, but not SphK2, is responsible for production of the S1P exported from breast cancer cells. These findings have important clinical implications as exported S1P may play an important role in breast tumor progression.

P-35: Monoclonal Antibody Against Transforming Growth Factor β Ligands Inhibits Bone Metastasis in a Preclinical Model

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Background: Transforming growth factor β (TGFβ) promotes breast cancer bone metastasis, by modulating both cancer cells and the bone microenvironment. Inhibiting TGFβ signaling by small molecule kinase inhibitors reduces tumor burden and bone lesions in preclinical bone metastasis models. However, nonspecific side effects of these compounds are not uncommon.

Objective: In this study, we tested the hypothesis that systemic administration of a pan-TGFβ antibody, 1D11(Genzyme corporation), might reduce tumor burden in bone.

Method: An experimental bone metastasis model was used for this study, where MDA-MB-231 human breast cancer cells were injected in 4–5-week-old female nude mice via the left cardiac ventricle. Tumor-bearing mice were treated with either 1D11 or control antibody (13C4) i.p. three times every week for 2 weeks. Treatment was initiated 2 weeks after tumor inoculation. Efficacy of 1D11 on metastatic progression of breast cancer cells in bone was tested using faxitron analysis of bone lesions, microCT analysis on bone volume, and histomorphometry to examine tumor burden in bone.

Results: Treatment with 1D11(10mg/Kg, three times a week for 2 weeks) reduced the number of bone lesions (Control: 7.4, Treated: 2.3, $P<.005$), and area of bone lesions (control: 7535.5 cm2, treated: 865.5 cm2, $P<.001$) and increased tibial bone volume (Control: 0.093, Treatment: 0.198, $P=.01$).

Conclusion: Anti-TGFβ antibody, thus, effectively reduces metastatic bone lesions in human breast cancer metastasis to bone. We are investigating the molecular mechanisms by which this anti-TGFβ antibody 1D11 reduces bone metastasis.

P-36: Breast Adipose Participates To Bioactivate Vitamin D3 and Inhibit Breast Cancer

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Background: Vitamin D3 is a nutritionally modulated hormone that participates as a negative growth regulator of mammary gland development and transformation. However, the mechanism behind tissue-specific vitamin D3 synthesis, metabolism, and signaling to maintain glandular homeostasis and inhibit the onset of mammary transformation remains unknown.

Objective: Our objective is to test the concept that vitamin D3 signaling in mammary adipose tissue contributes to the negative growth regulation of mammary epithelial cells. Our hypothesis is that the mammary adipose tissue bioactivates dietary 25-hydroxyvitamin D3 [25(OH)D3] to the active metabolite, 1a,25-dihydroxyvitamin D3 [1,25(OH)2D3], and induces adipocyte vitamin D3 receptor (VDR) signaling along with paracrine secretion of 1,25(OH)2D3 to surrounding mammary epithelial cells to regulate growth of normal and transformed breast epithelial cells.

Method: We utilized mammary glands from VDR knockout (KO) and wild type (WT) mice for various procedures including ex vivo co-cultures with mammary epithelium and adipocytes, gene and protein expression assays, immunohistochemistry, and whole mounts.

Results: Breast adipocytes express the essential signaling components of the vitamin D3 endocrine system and have the ability to bioactivate 25(OH)D3 to 1,25(OH)2D3 inducing mammary-specific vitamin D3-responsive gene expression, suggesting that mammary adipose tissue participates in maintaining localized vitamin D3 homeostasis and contributes to regulate the growth of mammary epithelial cells in response to various hormonal stimulations.

Conclusion: Our work suggests that breast adipose tissue serves as a vital endocrine mediator of vitamin D3 signaling and offers a possible mechanism by which elevated 25(OH)D3 serum concentrations reduce the susceptibility to breast cancer.

P-37: Potential Roles for CCL2 and CXCL1 Inflammatory Chemokine Signaling in Fibroblast: Mammary Carcinoma Cell Interactions

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Background: While diagnosis and treatment for breast cancer has improved over decades, metastatic spread remains a poorly understood disease with few treatment options. Studies have shown that stromal fibroblasts influence breast cancer cell growth and invasiveness through secretion of soluble factors. Data from our laboratory suggest that secretion of inflammatory chemokines from fibroblasts, in particular CCL2 and CXCL1, may significantly affect breast cancer progression. While studies have shown that chemokines regulate immune cell recruitment during inflammation, we hypothesize that chemokine signaling also regulates fibroblast interactions with carcinoma cells to mediate breast carcinoma growth and metastatic spread.

Objective: To analyze the functional contributions of CCL2 and CXCL1 signaling in fibroblast: epithelial interactions during breast cancer progression.

Method: Cultured mouse and human fibroblasts were subject to cDNA and protein array profiling and RT-PCR and ELISA analyses. Fibroblasts were co-cultured with carcinoma cells and analyzed for migration by transwell assays in the presence of neutralizing antibodies to CCL2 and CXCL1. Mouse fibroblasts were co-implanted with carcinoma cells into nude mice, treated with neutralizing antibodies to CCL2 and analyzed by histological and biochemical analyses.

Results: Expression profiling analyses show high-level expression of CCL2 and CXCL1 in mouse and human fibroblasts. Fibroblast-conditioned medium enhanced the migration and invasion of carcinoma cells, which was abrogated in the presence of CCL2 and CXCL1 neutralization. Tumor-bearing mice treated with CCL2 inhibitors showed significant decreased tumor growth and metastasis.

Conclusion: CCL2 and CXCL1 regulate fibroblast interactions with mammary carcinoma cells during tumor growth and metastasis.

P-38: Bombesin and Epidermal Growth Factor Increase Breast Cancer Cell Migration and Interleukin-8 Expression

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Background: Over-expression of members of the epidermal growth factor (EGF) family of receptor tyrosine kinases correlates with poor prognosis in breast cancer. In vivo and in vitro models of breast cancer have shown that BBS (amphibian) or gastrin-releasing peptide (GRP-mammalian) and their cognate receptor, GRP receptor (GRPR), promote cancer growth.

Objective: The aim of this study is to demonstrate that BBS and EGF cooperate to contribute to breast cancer progression.

Method: MDA-MB-231 breast cancer cells over-express both EGFR and GRPR. Cellular proliferation after treatment with BBS, EGF, or both was assessed in serum-starved cells by Coulter counter. Migration was performed using Transwell chambers. The migrated cells were fixed, stained, and quantified. Northern blot and real-time PCR were used to evaluate if proangiogenic factor interleukin-8 (IL-8) mRNA increased with addition of EGF, BBS, or both. Western blot for phosporylated ERK was used to assess activation of the mitogen-activated protein kinase (MAPK) pathway.

Results: Stimulation with EGF and BBS increased cell migration, phosphorylated ERK, and synergistically upregulated IL-8 mRNA, compared to no treatment, EGF, or BBS alone. However, with regard to cellular proliferation, no differences were found between cells treated with EGF, BBS, or the combination.

Conclusion: GRPR and EGFR cooperate to regulate cell migration, IL-8 expression, and MAPK activation, but not cell proliferation in MDA-MB-231 breast cancer cells. Identifying pathways that lead to hyperactivation of EGFR signaling, such as cooperative signaling by GRPR, is critical for improving rational design of combination drug regimens for breast cancer.

P-39: Cyclin D1 Can Act as a Positive or Negative Effector in AIB1-Mediated Tumorigenesis

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Background: AIB1 is a member of the p160 family of estrogen receptor (ER) transcriptional coactivators. We showed previously that over-expression of AIB1 in transgenic mice leads to mammary hypertrophy, hyperplasia, and a high incidence of multiple tumors involving mammary gland as well as pituitary, uterus, and lung. AIB1 over-expression resulted in increased cyclin D1 mRNA and protein levels.

Objective: To determine whether cyclin D1 is an effector of AIB1-induced oncogenesis.

Method: AIB1 transgenic mice were crossed with cyclin D1−/− mice to generate double mutant mice. Microscopic analyses of mammary gland development were performed using H&E stained whole mounts and immunohistochemical analysis of ER, AIB1, and cyclin D1 expression. Rates of tumor formation for various tumor types were determined.

Results: AIB1 over-expression did not rescue the cyclin D1−/− mammary gland phenotype, namely failure to reach the lobulo-alveolar phase of development during pregnancy in order to enable lactation. More importantly, unlike the AIB1 transgenic mice, double mutant mice did not develop mammary gland, uterus, pituitary, or lung tumors. Surprisingly, double mutants developed a high incidence of lymphomas. This tumor type was not observed in AIB1 transgenic mice or in cyclin D1−/− mice.

Conclusion: (1) Cyclin D1 is required for the formation of all tumor types observed in the AIB1 tumor model. Therefore, cyclin D1 is a downstream effector of AIB1. (2) Ablation of cyclin D1 in AIB1 transgenic mice leads to a high incidence of lymphomas, indicating that in certain tissue types cyclin D1 may act as a tumor suppressor.

P-40: Women Have Elevated Lipid Concentrations 8 Years After Preterm Births Not Complicated by Preeclampsia or Growth Restriction

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Background: Women with preterm birth (PTB) are at increased risk for cardiovascular disease (CVD), but mechanisms are not understood.

Objective: Women with spontaneous PTB have early gestation dyslipidemia, and we studied lipid aberrations post partum.

Method: Women who delivered preterm (<34 weeks, n=41; 34–<37 weeks, n=18) were compared to 183 women with term births (>=37 weeks). Women with preexisting medical conditions, preeclampsia or growth restriction, were excluded. Mean lipid concentrations at 8 years post partum were compared.

Results: Women with a prior preterm (pPTB) v. term birth had higher concentrations of total cholesterol, and women with pPTB <34 weeks had the highest concentrations (<34 weeks, 203.8.1; 34–<37 weeks, 188.8; =37 weeks, 183.7; p<0.01). Results were similar for apolipoprotein-B (APOB) and LDL. After adjustment for race, age, smoking, and body mass index, total cholesterol among women with pPTB <34 weeks was on average 19.3 mg/dl higher (p<0.01), LDL was 14.3 mg/dl higher (p=0.01), and APOB was 10.9 mg/dl (p<0.01) higher compared to women with term births. Women with pPTB were 3.0 (1.2, 7.8) times more likely to have cholesterol >240 and 2.7 times (95% CI 1.0, 7.4) more likely to have LDL >160 compared to women with term births, after covariate adjustment. Triglyceride concentrations tended to be higher in women with pPTB <34 weeks (p=0.09), but there were no differences in HDL.

Conclusion: Eight years post partum, women with a history of spontaneous pPTB had substantially elevated atherogenic lipid concentrations. Dyslipidemia may be a mechanism linking PTB to later CVD.

P-41: Identification of Critical Gel Properties for Describing Delivery of Vaginal Gels

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Background: Vaginally delivered microbicide gels need to cover and protect epithelial surfaces. Epithelial coverage is determined by a gel's physical properties and response to tissue squeezing forces. Our long-term goal is to optimize gel structure to yield ideal gel properties. However, first we need to identify what gel properties are critical for describing how a gel spreads due to squeezing. Previous studies indicate that viscometric power-law parameters (consistency and shear-thinning) do not sufficiently describe all squeezing flow experiments.

Objective: To determine if independently measured power-law parameters are sufficient to describe applied-rate squeezing flow experiments of a hydroxyethylcellulose (HEC) gel used in microbicide clinical trials as a "universal placebo." This study examines the effects of HEC concentration, squeezing rate, and squeezing configuration (constant-radius or constant-volume).

Method: We quantitatively evaluated the appropriateness of power-law parameters in two ways. First, previous viscometric measurements of power-law parameters were used as input to a mathematical squeezing model. Theoretical results were compared to previous experimental squeezing data using a goodness of fit measurement. Second, we fit the power-law parameters of the theoretical model directly to experimental squeezing data.

Results: For both rates and both HEC concentrations, power-law parameters adequately described constant-radius squeezing experiments, but not constant-volume squeezing experiments.

Conclusion: This is a new study evaluating constant-volume squeezing of HEC gels and has physiological relevance to vaginal delivery of the universal placebo. These data suggest that other properties, such as viscoelastic measurements, may be needed to describe constant-volume squeezing flows. Further studies will examine other concentrations, rates, and volumes.

P-42: Baseline Characteristics of the Participants of a Randomized, Double-Blind, Placebo-Controlled Trial of Atorvastatin for the Treatment of Women With Polycystic Ovary Syndrome

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Background: As LDL-cholesterol is the primary precursor for sex steroid synthesis, dyslipidemia may play a central role in the pathogenesis of polycystic ovary syndrome (PCOS). Many women with PCOS have mild to moderate dyslipidemia, but do not meet the current National Cholesterol Education Program indications for statin therapy. The specific aim of this project is to determine whether atorvastatin will improve the cardiometabolic phenotype of women with PCOS.

Objective: To report the baseline characteristics and metabolic profile of our study cohort.

Method: LDL-cholesterol was measured in 28 women with PCOS, ages 18–40 years. Seventeen women with PCOS and LDL-cholesterol >100 mg/dl were randomized to atorvastatin 40 mg daily or placebo for 6 weeks. Our primary outcome is change in brachial artery flow-mediated dilatation (FMD), a noninvasive measure of endothelial function. Major secondary outcomes include hormonal and metabolic profiles.

Results: LDL-cholesterol was >100 mg/dl in 20 of 28 (71%) women with PCOS. The mean (±SD) age of the randomized subjects was 31.9±4.2 years, and the mean body mass index was 38.3±12.2 kg/m2. The mean testosterone level was 74.9± 44.8 mg/dl. The mean LDL-cholesterol level was 130.8±24.9 mg/dl. One woman had elevated fasting glucose >100 mg/dl, and four women had elevated glucose 2 hours after a 75-gram oral glucose load. The mean fasting glucose-insulin ratio was 7.2±4.2. The mean baseline FMD was 12.8±6.3%.

Conclusion: Many women with PCOS have elevated LDL-cholesterol and may benefit from stain therapy.

P-43: Platelet Activation in Acute Ischemic Stroke: Gender Differences and Subtypes of Ischemic Stroke

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Background: Platelets are activated in acute ischemic stroke (AIS), and they secrete P-selectin, which potentiates vascular injury. Antiplatelet agents are recommended for secondary prevention of ischemic stroke. Thus, there are treatment implications if one can objectively prove that platelet activation differs in the subtypes of AIS. Postmenopausal women have unique characteristics related to ischemic stroke: increased incidence, higher morbidity and mortality, and poor response to antiplatelet agent. Whether this finding is related to hormonal differences or differences in inherent platelet function is not clear.

Objective: The purpose of this study is to measure the expression of P-selectin using flow cytometry in AIS patients to determine whether activation differs between gender and stroke subtypes.

Method: Whole blood samples were collected on AIS patients, and flow cytometry was performed to measure activation of platelets in men and women, and in two subtypes of AIS: large vessel atherosclerosis (LVA) and lacunar (LAC) strokes.

Results: Flow cytometry was performed on 40 patients. Of the 40 patients, 26 (13 females) had lacunar strokes, while 14 (4 females) were strokes caused by LVA. In this small sample study, there was no significant difference in the platelet activation between males and females. LVA strokes had a trend toward higher platelet activation than LAC strokes (P=.071).

Conclusion: Platelet activation differs in different subtypes of AIS, though larger studies are needed to substantiate the difference in platelet activation between subtypes of stroke. No gender differences in platelet activation were noted, though ongoing studies will confirm our results.

P-44: Familial and Gender Influences on Adolescent Weight Status: A Latent Class Analysis

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Background: Family meal frequency, family support for physical activity, parental modeling, and parenting style have been linked to healthful dietary behaviors and increased physical activity among youth. However, previous research has identified these factors almost in isolation of each other, and gender influences on these variables have been overlooked. Therefore, little is known about how these factors cooccur within families, and the influence of the coexistence of these factors within families on adolescents' behavior.

Objective: (1) Use latent class analysis to identify distinct classes of home environments based on the coexistence of multiple weight-related family factors. (2) Examine effects of gender differences between opposite-sex and same-sex parent-child dyads.

Method: Project EAT (Eating Among Teens) data, a population-based study (n=4746) of adolescents, was used to identify subtypes of home environments using adolescents' reporting of characteristics within the home. A latent class analysis was conducted with 23 measures of the home environment to identify distinct classes.

Results: Four classes of home environments were identified, each consisting of distinct combinations of levels of modeling and encouragement of physical activity and healthy dietary intake, parenting styles, and family meals habits. Father-daughter dyads were found to have higher levels of modeling and encouraging healthy dietary intake and physical activity versus mother-son dyads or same-gender dyads.

Conclusion: Developing home environment classes to understand how various weight-related factors coexist within families can provide new insight into the dynamics of the home environment and the influence of gender on adolescents' weight-related behaviors.

P-45: Insulin Resistance in Type 1 Diabetes Correlates With Coronary Artery Calcification

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Background: The mechanism of enhanced CVD risk in Type 1 diabetes (T1D) is unclear. Reports have suggested that individuals with T1D have decreased whole-body insulin sensitivity compared to those without diabetes (non-DM). Less is known about the antilipolytic effect of insulin or its role in CVD.

Objective: Measure insulin-mediated non-esterified fatty acid (NEFA) suppression in T1D and non-DM subjects, and correlate it to coronary artery calcification (CAC).

Method: As a substudy of the CACTI (CAC in T1D) study, a three-stage hyperinsulinemic-euglycemic clamp was performed to measure peripheral insulin sensitivity and suppression of NEFA levels in T1D and non-DM subjects.

Results: 54 subjects (39% T1D, 43% male; mean±SD: age=43±6, BMI=26.8±4.3) have been studied. Subjects with T1D were whole-body insulin resistant compared to non-DM controls (mean±SE glucose infusion rate [mg/kg/min]=3.59±0.85 v. 9.45±0.65, $p<0.0001$). NEFA suppression by insulin also differed by T1D status. At 4mU/m2/min of insulin, NEFA levels were suppressed by 39% among controls and increased by 63% in T1D subjects ($p<0.0001$), indicating adipose tissue insulin resistance (IR) in T1D. NEFA suppression was also impaired at 8mU/m2/min insulin (11% v. 69%, $p<0.0001$). Total CAC and CAC progression correlate with whole-body IR ($p=0.003$, 0.0007) and NEFA levels during clamp stages 1 ($p=0.05$, 0.04) and 2 ($p=0.01$, 0.005).

Conclusion: Subjects with T1D have decreased whole-body insulin action and insulin-mediated NEFA suppression compared to controls. NEFA levels in response to insulin correlate with CAC score and progression. These data suggest a mechanism by which IR could contribute to CVD risk.

P-46: Quantitative Metabolomics Reveals an Epi-Genetic Blueprint for Iron Acquisition in Uropathogenic Escherichia Coli

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Background: Urinary tract infections (UTIs) caused by uropathogenic E. coli (UPEC) disproportionately affect women and often recur following treatment. Genetic studies have suggested that the ability to cause UTI correlates with acquisition or alteration of genes for iron uptake, including those involved with siderophores—a chemically diverse family of small molecules that function as iron scavengers.

Objective: To use quantitative product analysis in a patient population with recurrent UTI to determine if UPEC secrete a characteristic siderophore profile when compared to coexisting rectal strains.

Method: We have developed a novel quantitative metabolomic approach based on stable isotope dilution mass spectrometry to compare siderophore production between clinical E. coli isolates. This method was applied to mutant strains, previously genotyped isolates, and a collection of PFGE-typed urinary and rectal isolates obtained through a SCOR collaboration with the University of Washington.

Results: Conventional PCR genotyping was not a reliable predictor of siderophore production. Differential siderophore expression between coexisting urinary and rectal E. coli strains in 13 recurrent UTI patients revealed strong preferential expression of the siderophores yersiniabactin and salmochelin by urinary strains. A linearized enterobactin siderophore was

also newly identified as a product of strains with active salmochelin genes.

Conclusion: These findings argue that qualititative and quantitative epigenetic optimization occurs in the E. coli secondary metabolome among human uropathogens. Because the virulence-associated biosynthetic pathways are distinct from those associated with rectal colonization, these results suggest strategies for virulence-targeted therapies.

P-47: Delayed Referral Does Not Explain Poor Outcomes in African-American Female Kidney Transplant Patients

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Background and Objective: African Americans (AAs) have worse graft survival than non-African Americans (NAAs) following kidney transplantation. A recent analysis from our center demonstrated that AA women have the greatest risk for graft failure. Evidence exists that referral rates for black women are low, but research is limited. The purpose of this study is to determine if prolonged time to referral explains poor outcomes in AA female kidney transplant recipients.

Method: Four-hundred and fifty-two patients who underwent an isolated kidney transplant between January 1996 and December 2004 were included in this retrospective review. Patients were grouped by ethnicity and gender (AA:NAA male, 135:126; and AA:NAA female, 103:88) and were followed for up to 3 years for graft failure or death. Patients receiving a preemptive transplant, a transplant prior to start of dialysis, were excluded.

Results: Kaplan-Meier estimation identified AA females having the lowest graft survival at all years, which persisted after adjustment for age, body mass index, and all other groups (hazard ratio: 2.6, 95% CI: 1.44, 4.2). Mean duration of time from diagnosis of end-stage renal disease or first dialysis until the time of transplant evaluation was calculated. Mean time (years) to evaluation for black women versus all other groups was 2.32 and 2.4, respectively ($p=0.83$). Multivariate adjustment was omitted due to lack of significance.

Conclusion: We speculate that it is largely the AA females negatively influencing outcomes in AA kidney transplantation. However, our results suggest that time to referral is not an impact factor in our population.

P-48: Rising Incidence of End-Stage Renal Disease (ESRD) Due to Systemic Lupus Erythematosus Among Blacks and Women

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Background: Systemic lupus erythematosus (lupus) is an autoimmune disease that can cause ESRD necessitating dialysis or renal transplantation. Recent changes in lupus ESRD incidence in different U.S. sociodemographic groups are unknown.

Objective: We aimed to investigate recent lupus ESRD incidence rates in different sociodemographic groups nationwide.

Method: We examined lupus ESRD incidence rates, 1995–2004, using the U.S. Renal Datasystem, enrolling all new ESRD patients. We calculated standardized incidence rates employing U.S. Census population estimates, stratified according to age, sex, race, and ethnicity.

Results: Lupus ESRD incidence rose from 3.0 to 3.9/million person-years from 1995 to 2004 in the United States. Women accounted for 82% of cases; the standardized incidence rate in women increased from 4.7 to 6.2/million person years. The 37% incidence increase among Blacks (10.5 to 14.4/million person-years) was higher than for other races and ethnicities. The proportion of Blacks among incident cases increased from 45% to 49%, exceeding that of Whites, which fell from 47% to 42%. In 2004, the standard incidence rates (per million person-years) were 14.4 among Blacks, 4.6 among Hispanics, 3.8 among Asians and Pacific Islanders, and 2.0 among Whites.

Conclusion: From 1995 to 2004, lupus ESRD incidence rose, disproportionately so among women and Blacks. For the first time, the incidence rate in Blacks surpassed that in Whites. The causes of these alarming disparities deserve further investigation

P-49: ARFI Ultrasound for Discrimination of Calcification in Arterial Plaques: Additional Progress Toward Improved Atherosclerosis Imaging in Women

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Background: While cardiovascular disease remains the primary killer of women in Western countries, decreasing death rates have been attributed to timely and appropriate treatments. However, treatment administration is limited by shortcomings in conventional atherosclerosis imaging technologies—they are not capable of detecting nonstenotic plaques and describing plaque material composition. These shortcomings may disproportionately impact women, who, recent evidence suggests, are predisposed to developing nonstenotic plaques. We previously demonstrated that a new imaging technology, Acoustic Radiation Force Impulse (ARFI) ultrasound, is capable of detecting nonstenotic plaques and of describing plaque elastin and collagen composition for risk assessment.

Objective: We now evaluate ARFI's potential for discriminating plaque calcium content, which is an established marker of atheromatous-plaque burden and is predictive of future risk of cardiovascular events.

Method: Two-dimensional ARFI and matched B-Mode imaging were performed in the left femoral artery of a female adult pig in the region of an advanced atherosclerotic plaque with calcification. The artery was then sectioned for validation by spatially correlated immunohistochemistry.

Results: In a region of calcium deposition in the context of diffuse atherosclerosis, median ARFI-induced peak displacement was 20% smaller compared to plaque tissue with no calcification. Shear Wave Elasticity Imaging (SWEI) derived shear wave velocity was 20% faster in the calcified region than in the adjacent plaque tissue.

Conclusion: Arterial calcium deposition was associated with smaller ARFI-induced peak displacement and faster SWEI-derived shear wave velocities in this pilot investigation. This supports ARFI's potential for noninvasive discrimination of arterial calcium content.

P-50: Health Disparities: Obesity, Pre-Diabetes, and Diabetes Among U.S. Latino, White Non-Latino, and Black Non-Latino Men and Women

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Background: Obesity, diabetes, and metabolic and nutritional disorders are major public health concerns for morbidity and

mortality for the Latino population. In the United States the estimated prevalence for obesity and overweight among 20- to 75-year-old Latina women is high, 71.9% and 46% respectively.

Objective: The objective of this study is to estimate the prevalence of obesity, diabetes, and pre-diabetes among a nationally representative sample of Mexican-American, White (non-Latina) and Black (non-Latina) women, using the National Heath and Nutrition Examination Survey (NHANES) data set.

Method: The data from the NHANES were used to examine the relationship between obesity, pre-diabetes, and diabetes (NCHS 2008b). Data used for this analysis included the 1999–2000, 2001–2002, 2003–2004, and 2005–2006 public use data files. The NHANES uses a complex probability survey design and sample weighting methodology.

Results: While more men than women were overweight, the prevalence of obesity among women was higher than for men in all three racial/ethnic groups. The prevalence of pre-diabetes was higher among White non-Latino men (17.89%) and Latino men (20.95%). In comparison, the prevalence of diabetes was highest among Black non-Latina women (5.04%) and White non-Latino males (4.02%), and similar for Latino men and women (4.56% and 4.41%, respectively).

Conclusion: The results from the NHANES data indicate gender differences in obesity, overweight, pre-diabetes, and diabetes among the three racial/ethnic groups studied. In particular, Black and Latina women had higher prevalence of diabetes and obesity. These findings have important implications for culturally specific prevention activities.

P-51: General and Abdominal Adiposity and Risk of Stroke in Chinese Women

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Background: Although both general and abdominal adiposity are well-established risk factors for coronary heart disease, their associations with stroke are less well characterized, particularly in Asian populations.

Objective: To evaluate the associations of body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio with stroke risk in the Shanghai Women's Health Study, an ongoing, population-based, prospective cohort study of 74,942 Chinese women ages 40–70 at recruitment in 1996–2000.

Method: For this analysis, we included 66,720 women who reported no prior history of stroke, coronary heart disease, rheumatic heart disease, cardiac surgery, or cancer, and who had anthropometric measures taken at recruitment. Incident cases of stroke were ascertained by biennial home visits and linkage with the vital statistics.

Results: During a mean followup of 7.3 years, 2,364 strokes occurred. BMI, WC, WHR, and waist-to-height ratio were all positively and significantly associated with the risk of total, ischemic, and hemorrhagic stroke. The multivariable-adjusted hazard ratios (95% confidence intervals) for total stroke comparing the highest v. lowest quintiles of these measurements were 1.74 (1.51–2.00), 1.80 (1.56–2.09), 1.63 (1.40–1.89), and 1.98 (1.66–2.35) for BMI, WC, WHR, and waist-to-height ratio, respectively. These positive associations were attenuated after additional adjustment for potential biological mediators, especially hypertension. We found no evidence of effect modification by age, menopausal status, exercise, or cigarette smoking.

Conclusion: Both general and abdominal adiposity independently predict stroke risk in Chinese women. These data reinforce the need to incorporate both body weight and fat distribution measurements in assessing stroke risk.

P-52: Rural African-American Women with Type-2 Diabetes View Motivational Interviewing as Less Effective Than Traditional Behavioral Counseling

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Background: Motivational interviewing (MI), a patient-centered method for enhancing a patient's motivation for behavioral change, has been the main intervention strategy in many studies to improve behavioral and health outcomes of patients with type-2 diabetes. The success of such interventions is highly dependent on patient acceptance of MI principles and strategies. However, little research has assessed patients' perceptions of MI prior to intervention implementation.

Objective: This study evaluated MI perceptions among rural African American women with type-2 diabetes.

Method: Four moderator-led focus groups were conducted with patients ages 21–50 who had never participated in an MI-focused behavioral intervention. Patients were asked to share general perceptions and perceived advantages and disadvantages of MI after viewing a patient/healthcare provider MI consultation; from a DVD series entitled *Motivational Interviewing: Professional Training Series*. Content-based data analysis of focus group transcripts was conducted using qualitative data analysis software, Atlas.ti., and analyst coding.

Results: Thirty patients participated. Two themes described perceived advantages of MI: (1) good communication and (2) active patient involvement. The patient-centeredness of the consultation was the single theme that described perceived disadvantages. Correspondingly, compared to MI, patients agreed that physician-led interactions (i.e., physician-led goal setting, limited patient input) were more representative of "good counseling" and also were most familiar to them.

Conclusion: These findings suggest that patients have both negative and positive views of MI. Future studies should assess whether patient satisfaction with MI interventions influences study protocol adherence and behavioral and health outcomes.

P-53: Female Obesity and Utilization of Fertility-Related Services

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Background: The increasing prevalence of obesity is a critical public health problem for women of childbearing age, as obesity can impair a woman's ability to conceive and increase her risk for an adverse pregnancy outcome. Yet, there is a paucity of information on whether utilization of fertility-related services varies according to female body mass.

Objective: To assess the relationship between female body mass index (BMI) and the utilization of fertility-related care in the United States.

Method: Data from the 2002 National Survey of Family Growth were examined to compute percentages for various fertility-related services, stratified by BMI categories.

Results: Obese women (11.5%) were more likely than underweight/normal (9.5%) and overweight (8.7%) women to report that they (or their partner) ever received fertility-related services. Advice, infertility testing, and drugs to improve ovulation were the most common services received across BMI categories. When infertility testing was performed, 31% of obese women reported that they alone underwent testing, compared to 18% of overweight women and 25% of underweight/normal women. The proportion of women who underwent artificial insemination varied from 12% in obese women to 16% in overweight women. "Problems with ovulation" was the most frequently reported diagnosis across the BMI categories, especially among obese women (44%).

Conclusion: Subtle differences exist in the utilization of fertility-related services according to female body mass; however, these disparities do not appear to be as consistent with increasing BMI.

P-54: Obesity and Women's Fertility Over the Life Course

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Background: Obesity is one of the most serious public health problems facing women today. This indicator of health status has important biological and social components, which has led scientists across disciplines to demonstrate obesity's links to the proximate determinants of fertility. As such, the negative consequences of obesity may accumulate over the life course leading obese young women to be stratified into disadvantaged positions for childbearing.

Objective: This study asks whether obesity is associated with young women's life course fertility experiences. The authors hypothesize that compared to their non-obese counterparts, obese young women have fewer live births, a higher risk of remaining childless, and later timing of first birth.

Method: Twenty-three years of data from National Longitudinal Survey of Youth: 1979 (NLSY:79) female respondents ages 20–24 in 1981 are analyzed to test these hypotheses using descriptive statistics, logistic regression methods, and event history analyses.

Results: All hypotheses are supported. On average, obese women have fewer children than non-obese women. Furthermore, compared to normal weight women, obese women's odds of remaining childless are almost three times as high after models include confounders. Obese women's lower parity may be explained by their later timing of first birth. Their hazard of first birth is over two times lower than normal weight peers after statistical models account for confounders.

Conclusion: Results confirm obese young women's position of disadvantage for childbearing and show that the negative consequences of obesity accumulate across a life domain that is incredibly important for the vast majority of American women.

P-55: Birth Size and Adult Metabolic Syndrome: Interaction With Race and Sex

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Background: Fetal growth retardation has been associated with the adult development of metabolic syndrome (MS). Some studies also suggest that high birthweight is also associated with higher risk.

Objective: To examine the associations between birth size and metabolic syndrome, including interaction by race and sex

Method: Birth certificate data were linked to records of participants in the Bogalusa Heart Study. Metabolic syndrome was defined by the National Cholesterol Education Program definition. Low birthweight was defined as birthweight<2500 g; macrosomia as birthweight >4000 g; SGA as birthweight $<10^{th}$ percentile for gestational age; and LGA as birthweight $>90^{th}$ percentile for gestational age. Logistic regression was used to adjust for smoking, alcohol use, income, home ownership, parental education, age, race, and sex.

Results: No association was seen between birth factors and MS (adjusted odds ratio [OR] for LBW 1.17, 95% confidence interval [CI] 0.61–2.24; for macrosomia, 0.80, 0.46–1.39; for SGA, 1.34, 0.76–2.38; for LGA, 0.96, 0.62–1.49). No interaction was seen with race. The risk associated with being small at birth was generally stronger for men than women; however, associations were imprecise. However, being too large was associated with an increased risk of MS for men (LGA, 1.54, 0.80–2.98), but a decreased risk for women (0.70, 0.39–1.26).

Conclusion: In this cohort, the relationship between both high and low birthweight and MS was not seen. The relationship between birthweight and MS may be stronger in men than women.

P-56: Gender Differences in BMI and Health-Related Quality of Life Among Older Mexican Americans

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Background: Obesity is a major health problem associated with morbidity, disability, and reduced quality of life.

Objective: Examine gender differences between body mass index (BMI) and health-related quality of life (HRQoL) in Mexican-American older adults. Also, examine the mediating effect of physical function and medical conditions on the association between obesity and HRQoL.

Method: Cross-sectional study of 830 Mexican-American men and women aged >75 residing in five southwestern States in the United States. Data were collected on sociodemographic variables, physical function, medical conditions, BMI, and the Medical Outcomes Study Short Form Health Survey (SF-36).

Results: Out of 830 subjects, 28.6% of women and 19.7% of men had a BMI=30 kg/m2. Mean score for the Physical Composite Scale (PCS) of the SF-36 was 34.24 (SD=11.33) in obese women and 41.32 (SD=10.4) in obese men. In a multiple regression analysis, an interaction effect between gender and BMI on the PCS was found (β=-0.38, $p<0.001$). Analysis by gender found that high BMI (=30 kg/m2) in women was significantly associated with lower scores on the PCS, while in men was not significantly associated with the PCS. The association between BMI=30 kg/m2 and the PCS in women was partially mediated by physical function and medical conditions. No significant association was found between high BMI and the Mental Composite Scale (MCS) of the SF-36 in men or women.

Conclusion: High BMI was associated with lower HRQoL in older Mexican-American women. No association was found between high BMI and HRQoL in men.

P-57: Gender Differences in Mortality Among Older Frail Mexican Americans

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Objective: To examine the association between frailty and 10-year mortality among older men and women of Mexican-American origin.

Method: Data were collected from 1995/1996 to 2004/2005 among community-dwelling Mexican Americans 65 years and older as part of the Hispanic Established Population for the Epidemiologic Study of the Elderly. A standardized frailty index based on weight loss, exhaustion, grip strength, walking speed, and physical activity was computed. Data were collected on sociodemographics and health characteristics, comorbidities, and performance-based functional measure.

Results: The sample was 58% female and mean baseline age was 74.5 years (SD=6.06) at baseline. Hazard ratios (HR) indicated an increased mortality risk in frail men (HR=3.04, 95% CI 2.16, 4.28) compared to frail women (HR=1.92, 95% CI 1.39, 2.65).

Conclusion: Frailty is an independent predictor of mortality among older men and women of Mexican-American origin. This association was found to be stronger among men.