# 2009 ISSWSH ABSTRACTS

## Paper Presentations

### #1

## BIOLOGY BASIC SCIENCE PRIZE ESSAY: ENDOTHELIN-1 INDUCES CONSTRICTION OF FEMALE PUDENDAL ARTERY THROUGH ETA RECEPTOR AND RHO-KINASE ACTIVATION: POTENTIAL ROLE IN FEMALE SEXUAL DYSFUNCTION

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**Introduction:** Endothelin-1 (ET-1), a potent vasoconstrictor peptide, acts mainly through the G-protein-coupled ETA receptor (ETAR). Increased ET-1 constrictor sensitivity has been observed in various cardiovascular diseases, including hypertension, as well as erectile dysfunction. The pudendal artery supplies blood to the vagina and clitoris. Inadequate blood flow through the pudendal artery leads to vaginal engorgement and clitoral erectile insufficiencies.
**Aim:** Characterize the effects of ET-1 on the pudendal artery.
**Methods:** Pudendal arteries from female Sprague Dawley rats (225–250 g) were mounted in microvessel chambers, maintained at 37°C. Segments were then submitted to increasing concentrations of ET-1 (10–10 to 10–6 M). Some segments were incubated with the ETAR antagonist, atrasentan (10–8 or 10–6 M) or the Rho-Kinase inhibitor, Y-27632 (10–6 M) 30 min prior to agonist exposure. Actions mediated through the ETBR were assessed using a specific agonist, IRL-1620 (10–10 to 10–6 M). mRNA of preproET-1, ETAR and ETBR from pudendal arteries were measured by real time PCR. All Emax values are expressed as % KCl max.
**Main Outcome Measures:** Constrictor sensitivity of pudendal arteries were assessed by concentration response curves to ET-1 and IRL-1620. Messenger RNA levels of preproET-1, ETAR and ETBR were measured.
**Results:** ET-1 constricted pudendal arteries concentration dependently (143.33 ± 8.28; pD2 = 7.49 ± 0.1) while pretreatment with atrasentan concentration dependently decreased ET-1-induced contraction (10–8 M, 76.67 ± 20.84, pD2 = 5.44 ± 033; 10–7 M, 31.69 ± 21.05, pD2 = 6.33 ± 1.44). Pretreatment with Y-27632 reduced ET-1 effects (101.25 ± 11.6; pD2 = 7.06 ± 0.19). IRL-1620 caused a modest constriction of pudendal arteries (37.97 ± 3.787, pD2 = 8.64 ± 0.4). Pudendal arteries contain the message for preproET-1, ETAR and ETBR.
**Conclusion:** We showed that the pudendal artery, essential in vaginal and clitoral blood flow, is sensitive to ET-1, signals through the ETAR and activates Rho Kinase. As well, ETBR are involved in the constriction of this artery, however to a lesser degree through ETAR. These data indicate ET-1 may play a role in impaired vaginal and clitoral blood flow in pathologies where ET-1 levels are elevated.
**Funding:** NIH.

### #2

## PSYCHOLOGY BASIC SCIENCE PRIZE ESSAY: PAIN CORRELATES IN WOMEN WITH PROVOKED VESTIBULODYNIA: EXAMINING THE RELATIONSHIP BETWEEN PSYCHOSOCIAL AND PSYCHOPHYSICAL FUNCTIONING

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**Introduction:** Provoked Vestibulodynia (PVD) is characterized by a sharp and burning pain localized to the vulvar vestibule. Research indicates that PVD stems from and is maintained by a complex combination of factors, including psychosocial and psychophysical functioning. While much research in the area of PVD is conducted with the aim of understanding the involvement of both these processes, only one study to date explicitly examined the relationship between these variables in women with PVD. Findings from this study suggested that increases in experimental pain catastrophizing were associated with lower pain thresholds and higher pain ratings in response to painful stimulation of the forearm and to increases in reported pain ratings during intercourse.
**Aim:** The aim of the present study was to investigate correlations between psychosocial (somatization and catastrophization), psychosexual (sexual self-efficacy and function), and psychophysical functioning (vulvar and non-vulvar pain sensitivity) in women with and without PVD.
**Methods:** Potential participants completed a screening interview and standardized gynecological examination to determine eligibility. Eligible women then completed an interview, questionnaires, and quantitative sensory testing (QST) session.
**Main Outcome Measures:** The Physical Component Summary of the Short-Form-36 Health Survey (PCS-SF-36; Ware & Sherbourne, 1992), the Pain Catastrophizing Scale (PCS; Sullivan et al., 1995), the Sexual Self-Efficacy Scale for Female Function (SSES-F; Bailes et al., 1989), the Female Sexual Function Index (FSFI; Rosen et al., 2000), and pressure-pain and thermal QST at the forearm and the vulva.
**Results:** When compared to controls, women with PVD displayed lower pain thresholds, higher pain ratings, lower sexual functioning and sexual self-efficacy, and higher levels of somatization and catastrophization. In women with PVD, higher sexual self-efficacy correlated significantly with better sexual functioning, and higher somatization was associated with more catastrophizing. Over the entire sample, lower psychosocial functioning was correlated with decreased vulvar pressure-pain thresholds and increased cotton-swab test pain ratings. In the PVD sample, decreased sexual function and sexual self-efficacy were also associated with higher vulvar pressure-pain ratings.
**Conclusions:** Results indicate that women with PVD would benefit from treatment that addresses pain-focused and psychosocial components.

### #3

## ESTRADIOL AMELIORATES DIABETES-INDUCED CHANGES IN VAGINAL STRUCTURE OF DB/DB MOUSE MODEL

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**Introduction:** Diabetes plays a principal role in the etiology of sexual dysfunction. Women with diabetes experience diminished genital

arousal, reduced vaginal lubrication, vaginal atrophy, dyspareunia, and increased infections. Limited studies are available investigating the effects of diabetic complications on the vagina.
**Aim:** The goals of this study were to investigate type 2 diabetes-induced changes in vaginal structure and to determine if estradiol treatment ameliorates these changes.
**Methods:** Eight week-old female diabetic (db/db) mice (strain BKS. Cg-m +/+ Leprdb/J) and age-matched control normoglycemic female littermates were used to investigate the effects of type 2 diabetes on vaginal tissue structural integrity. Diabetic animals were divided into two subgroups: diabetic treated with vehicle only and diabetic treated with pellets containing estradiol. At 16 weeks, animals were sacrificed, the vaginal tissues excised and analyzed by histological and immunohistochemical methods to assess diabetes-induced changes in vaginal tissue and the extent by which these parameters are restored by estradiol treatment.
**Main Outcome Measures:** The main outcome measure was to quantitate diabetes-induced changes in vaginal histoarchitecture and the effects of estradiol treatment on these changes.
**Results:** Diabetic animals exhibited high blood glucose levels (>600 mg/dl), increased body weight and reduced plasma estradiol levels when compared to control animals. Diabetes resulted in significant thinning of the epithelium, marked decrease in the muscularis area, distinct truncation of elastic fibers, and significant reduction of the nitrergic immunoreactive nerve fibers. Treatment of diabetic animals with estradiol restored epithelial thickness, muscularis area, elastic fiber distribution, and partially restored the density of nitrergic nerve fibers.
**Conclusions:** The data in this study demonstrate that type 2 diabetes disrupts vaginal structural integrity and that estradiol supplementation ameliorates the diabetes-induced vaginal pathology.

**#4**

## ANTIDEPRESSANT TREATMENT REDUCES BEHAVIORAL INDICES OF DEPRESSION IN A RAT MODEL OF POST-PARTUM DEPRESSION

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**Introduction:** Post-partum depression in women has been linked to high levels of hormones present during late pregnancy and dropping precipitously post-partum. Previously, we reported an animal model of this depressive response to high levels of hormones followed by withdrawal. In this model we found evidence of depression-like behavior in two established behavioral tests: [1] the social interaction test (SI) in which social interactions and activity are documented, and [2] the forced swim test (FST) in which time spent immobile is an index of depression. In the present study we addressed the question of whether treatment with desipramine could mitigate the depressogenic effects of the hormone treatment.
**Methods:** Rats were treated for 23 days with 4 mg progesterone. For the first 16 days of this treatment regime, they also received 2.5 μg estrogen, followed by 7 days of 50 μg estrogen. These rats were then divided into three groups: those that received desipramine (5 mg/kg daily for 8 days), another thyroid hormone (250 ug/kg for 8 days), and a third vehicle (1 ml/kg for 8 days). Control animals received vehicle injections throughout the experiment.
**Results:** In the SI test, the control animals exhibited more social interaction and activity, and in the FST less immobility than the hormone-pretreated rats. The group that received hormone treatment plus desipramine exhibited higher levels of social interaction compared to the hormone treatment alone. Moreover, the hormone plus desipramine group did not differ from non-hormone–treated control animals ($F = 4.142$, 3/40 df, $P = .012$), indicating a return to normal behavior. Hormone treated rats given desipramine also had fewer line crossings than the other groups ($F = 10.625$, 3/40 df, $P < .001$). In the FST, the hormone plus desipramine group reversed the increased immobility seen with hormone treatment alone, back to baseline levels ($F + 7.860$, 3/40 df, $P < .001$).
**Conclusion:** In conclusion, both the social interaction deficits and increased immobility in the FST evoked by hormone treatment, were mitigated by administration of the antidepressant, desipramine. This extends this rat model of post-partum depression by documenting that the depressogenic effect of estrogen + progesterone treatment, mimicking hormone changes associated with pregnancy and parturition, respond to antidepressant treatment.

**#5**

## UNDERSTANDING VAGINAL INNERVATION: A PSEUDORABIES VIRUS RETROGRADE TRACER STUDY

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**Introduction:** The vagina is an essential organ that allows for sexual arousal, parturition, and an excretory duct for menstrual flow. Dyspareunia, secondary to vaginal dryness is a common problem that occurs with menopause as estrogen levels decline. An ovariectomized rat model was used to study vaginal innervation during a simulated state of menopause.
**Objective:** This study examined the spinal and brain circuits that regulate the vagina with the hope that the gathered evidence may be useful for understanding physiological and neural changes that occur in women who have sexual arousal disorders that may be related to vaginal function.
**Methods:** Pseudorabies virus (PRV) was injected into the distal corpus vagina of sexually experienced, ovariectomized Sprague-Dawley rats. 4 to 5 days later the brain and spinal cord were collected and processed for immunocytochemical identification of retrogradely labeled neurons. PRV-containing cells were counted in each segment and categorized into dorsal horn, ventral horn, and medial, lateral and intermediate gray.
**Results:** PRV successfully infected the spinal cord and specific nuclei in the brain. After 4 days, PRV cells were found primarily in L5-S1, with fewer cells distributed in T11-L4. Most of the neurons in L5-S1 were located in the medial (dorsal gray commissure) and lateral gray including the parasympathetic preganglionic neurons. PRV cells were also present in T10-L2 in the intermediate, lateral and medial gray with fewer cells in L3-L4. In some animals more PRV cells were found in thoracic regions, which may be related to different injection sites within the vagina. After 5 days, a significantly higher number of cells were found throughout the spinal cord, with relative paucity in the ventral horns. Dorsal horn neurons were labeled only after longer survival times. In the brain, PRV cells were found in areas commonly shown to innervate the pelvic organs.
**Conclusion:** The present study demonstrates that PRV can be used to elucidate the neural innervation of the vaginal wall of female rats. Early infection of the medial and dorsal gray commissure of L5-S1, suggests the importance of parasympathetic projections to the vagina. However, PRV cells in the thoracic cord also underlie the presence and importance of a sympathetic innervation. Longer survival times resulted in increased projections to spinal cord circuits in T10-S3, with little ventral horn (motor) projections, thus suggesting T11-S3 segments serve an important sensory role in the innervation of the vaginal wall.

**#6**

## DOES THE LEVEL OF PHYSICIAN TRAINING IMPACT SEXUAL HISTORY TAKING?

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**Introduction:** Experience of sexual concerns by women is common and they often seek advice from primary care physicians (PCPs) and