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This newsletter is quarterly and contains abstracts from medical journals published between June and December 2005 (abstracts presented at scientific meetings may also be included). Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia / Pain

Effects of intradermal foot and forearm capsaicin injections in normal and vulvodynia-afflicted women.

Foster DC, Dworkin RH, Wood RW

Pain, Volume 117, Issues 1-2, September 2005, Pages 128-36.

Cutaneous response to capsaicin has been used to assess central sensitization in pain research. This study compared the response to intradermal capsaicin in the forearm and foot of vulvar vestibulitis (vestibulodynia)-afflicted cases and controls. We hypothesized that cases will experience greater spontaneous pain, larger cutaneous areas of punctate hyperalgesia and dynamic allodynia, and greater vascular flow than controls. We also hypothesized enhanced post-injection pain in the foot compared to the forearm based on dermatome proximity of the foot and vulva. Methods. Ten vulvar vestibulitis syndrome (VVS) cases and 10 age and ethnically matched controls underwent two randomized, cross-over trials with intra-dermal injections of capsaicin or a saline placebo in the forearm and foot. Outcome measures included spontaneous pain level, surface area of punctate hyperalgesia, surface area of dynamic allodynia, cutaneous blood flow, regional skin temperature and vital signs. Results. VVS cases experienced greater spontaneous pain, punctate hyperalgesia and dynamic allodynia than pain-free controls. Within the VVS group, post-capsaicin spontaneous pain, punctate hyperalgesia and dynamic allodynia were similar in the forearm and foot. Post-capsaicin blood flow did not differ between cases and controls by anatomic site. Measures of depression and anxiety correlated with spontaneous pain intensity but did not correlate with measures of hyperalgesia, allodynia, or blood flow. VVS cases had higher resting pulse rates and lower resting systolic blood pressures than in controls. Conclusion. VVS patients show enhancement of post-capsaicin pain response extending far beyond the anatomic location of the primary complaint.

Vulvodynia: Strategies for treatment.

Goldstein AT, Marinoff SC, Haefner HK

Clin Obstet Gynecol 2005 Dec;48(4):769-785

Successful treatment of persistent vulvodynia with submucous infiltration of betamethasone and lidocaine.

Dede M, Yenen MC, Yilmaz A, Baser I

Eur J Obstet Gynecol Reprod Biol. 2005 Oct 25; [Epub ahead of print]

Insight into the treatment of vulvar pain: a survey of clinicians.

Updike GM, Wiesenfeld HC

Am J Obstet Gynecol. 2005 Oct;193(4): 1404-9

OBJECTIVE: The purpose of this investigation was to determine practice patterns among clinicians who frequently treat patients with vulvar pain syndromes. **STUDY DESIGN:** A cross-sectional survey was distributed to providers in the United States whose names were on a referral list of clinicians that care for women with vulvar pain (National Vulvodynia Association, Silver Springs, MD). The survey included 2 clinical vignettes. Clinicians were asked to report what treatments they would use to treat women with generalized vulvodynia and localized vulvodynia. Data were analyzed with descriptive statistics. A comparison of categorical data was accomplished with the Fisher's exact test. **RESULTS:** Surveys were mailed to 327 providers; 167 completed surveys were returned, for an overall response rate of 51%. The most commonly used treatment for vulvodynia was tricyclic antidepressants. There was no difference in the use of physical therapy, estrogens, injected or topical steroids, interferon, or laser therapy to treat generalized and localized vulvodynia. Respondents were more likely to use tricyclic antidepressants ($P < .001$), gabapentin ($P < .001$), and psychiatric care ($P < .001$) and less likely to use local anesthesia ($P < .001$) and vestibulectomy ($P = .007$) for the clinical scenario that represented generalized vulvodynia than they were for the scenario that represented localized vulvodynia. Most clinicians reported screening for vaginal infections, and many clinicians perform colposcopy and/or vulvar biopsy. Respondents recommend a variety of lifestyle modifications in the treatment of vulvodynia. **CONCLUSION:** Clinicians use a wide variety of treatments for vulvar pain and use different therapies for variants of vulvodynia.

Capsaicin for the treatment of vulvar vestibulitis.

Steinberg AC, Oyama IA, Rejba AE, Kellogg-Spadt S, Whitmore KE

Am J Obstet Gynecol. 2005 May;192(5):1549-53

Objective: The purpose of this study was to evaluate the use of local capsaicin cream as an effective treatment for patients with documented vulvar vestibulitis syndrome. **Study design:** A retrospective chart review was performed for patients who received a diagnosis of vulvar vestibulitis syndrome that was treated with capsaicin. Patients performed local application of capsaicin 0.025% cream for 20 minutes daily for 12 weeks. A comparison was made between the pre- and posttreatment Kaufman touch test to evaluate discomfort. The Marinoff dyspareunia scale was also used to assess pre- and posttreatment. **Results:** The sum of the Kaufman touch test scores before the treatment (13.2 +/- 4.9) compared with the scores after treatment (4.8 +/- 3.8) was statistically improved ($P < .001$). A significant improvement was also observed at each individual site ($P < .001$). The Marinoff dyspareunia scale also showed a significant improvement ($P < .001$). **Conclusion:** Vulvar vestibulitis syndrome that is treated with capsaicin significantly decreases discomfort and allows for more frequent sexual relations.

Cutaneous hypersensitivity to Candida albicans in idiopathic vulvodynia.

Ramirez De Knott HM, McCormick TS, Do SO, Goodman W, Ghannoum MA, Cooper KD, Nedorost ST
Contact Dermatitis. 2005 Oct;53(4):214-8

We have observed that the majority of our vulvodynia patients give a previous history of vaginal candidiasis that was treated but was followed by symptoms of chronic vulvodynia. 27 vulvodynia patients were patch-tested to a standard series of contact allergens, a customized vulvar series and commensal organisms including ultraviolet-killed *Candida albicans*. Comparison tests for the commensal organism were made to a group of 13 female atopic dermatitis patients and to 19 female dermatitis patients without a history of childhood flexural dermatitis who were undergoing patch test evaluation in our clinic. Patients reporting vulvodynia were significantly ($P < 0.05$) more likely to react to *C. albicans* than the dermatitis comparison group. Interestingly, lower concentrations of *C. albicans* caused more positive patch tests than higher concentrations. Our findings suggest that previous *C. albicans* infection may predispose patients to a subsequent hypersensitivity response to *C. albicans* that is expressed only in areas of high cutaneous peripheral fibre density. Low levels of *C. albicans* may also be required to elicit this response

as high levels of *C. albicans* may actually result in decreased cutaneous inflammation and decreased intensity of *C. albicans* patch test responses.

Pelvic floor muscle functioning in women with vulvar vestibulitis syndrome.

Reissing ED, Brown C, Lord MJ, Binik YM, Khalife S
Psychosom Obstet Gynaecol. 2005 Jun;26(2):107-13

Vaginal sEMG biofeedback and pelvic floor physical therapists' manual techniques are being increasingly included in the treatment of vulvar vestibulitis syndrome (VVS). Successful treatment outcomes have generated hypotheses concerning the role of pelvic floor pathology in the etiology of VVS. However, no data on pelvic floor functioning in women with VVS compared to controls are available. Twenty-nine women with VVS were matched to 29 women with no pain with intercourse. Two independent, structured pelvic floor examinations were carried out by physical therapists blind to the diagnostic status of the participants. Results indicated that therapists reached almost perfect agreement in their diagnosis of pelvic floor pathology. A series of significant correlations demonstrated the reliability of assessment results across muscle palpation sites. Women with VVS demonstrated significantly more vaginal hypertonicity, lack of vaginal muscle strength, and restriction of the vaginal opening, compared to women with no pain with intercourse. Anal palpation could not confirm generalized hypertonicity of the pelvic floor. We suggest that pelvic floor pathology in women with VVS is reactive in nature and elicited with palpations that result in VVS-type pain. Treatment interventions need to recognize the critical importance of addressing the conditioned, protective muscle guarding response in women with VVS.

Vulvar vestibulitis syndrome: A review.

Farage MA, Galask RP
Eur J Obstet Gynecol Reprod Biol. 2005 May 28; [Epub ahead of print]

Vulvar vestibulitis syndrome (VVS) is a perplexing disease involving pain limited to the vulvar vestibule without objective clinical findings to explain the symptoms. The condition impairs sexual function and creates significant psychological distress. Its cause is unknown, and few randomized studies exist on the efficacy of interventions. This article reviews disease characteristics, possible etiologies, and approaches to management.

When sex hurts, anxiety and fear orient attention towards pain.

Payne KA, Binik YM, Amsel R, Khalife S
European Journal of Pain, Volume 9, Issue 4, August 2005, Pgs 427-36

Hypervigilance for pain-relevant stimuli has been associated with anxiety, fear of pain and anxiety sensitivity. This attentional bias has been primarily investigated in heterogeneous pain groups or pain-free controls, but has not been examined in pain conditions where anxiety and fear are likely to play a central role. Due to the intimate and interpersonal nature of genital pain experienced during sexual intercourse, Vulvar Vestibulitis Syndrome (VVS) constitutes an ideal sample in which to investigate the role of cognitive and affective factors in pain perception and maintenance. Seventeen women suffering from VVS and an equal number of age and education matched control women completed an emotional Stroop and memory recall task in addition to a series of questionnaires assessing pain-hypervigilance, state and trait anxiety, fear of pain, and anxiety sensitivity. VVS sufferers reported hypervigilance for coital pain and also exhibited a selective attentional bias towards pain stimuli on the emotional Stroop task as compared with controls. This effect was predicted by state and trait anxiety and fear of pain. According to these data, treatment strategies for VVS should target anxiety and fear in addition to sensory systems.

IgE-Mediated allergy against human seminal plasma.

Weidinger S, Ring J, Kohn FM
Chem Immunol Allergy. 2005;88:128-38

Human seminal plasma hypersensitivity has to be differentiated from allergic reactions to latex, spermicidal agents, local anesthetics or components of lubricants. The present review article discusses IgE-mediated allergic reactions (type I) to specific components of the seminal plasma. Such incidents are rare, even though there seems to be a considerable number of unreported cases. Since the first publication in 1958, human seminal plasma allergy has been increasingly recognized, and approximately 80 cases have been described. Most affected women are younger than 40 years, presenting with an atopic family history. Anaphylaxis to components of the seminal plasma is not always associated with infertility. Complaints occur immediately or within 1 h after contact with seminal plasma. Local reactions include itching, burning, erythema and edema in the vulvar region or other sperm contact sites. Systemic reactions are experienced as dyspnea, dysphagia, rhinoconjunctival complaints, generalized urticaria, angioedema, gastrointestinal symptoms, exacerbation of existing atopic eczema or anaphylactic shock. Recently, it has been reported that human seminal plasma anaphylaxis may also present as 'vulvar vestibulitis syndrome' or 'burning semen syndrome'. These symptoms may occur during the first sexual intercourse. Some results are indicative of allergens originating from the prostate, prostate-specific antigen being clinically relevant. The diagnosis of human seminal plasma allergy is based on history, demonstration of specific IgE antibodies in the serum and skin tests. Therapeutic options include allergen avoidance by use of condoms and attempts at desensitization.

Vulvar disease: A pelvic floor pain disorder?

Kennedy CM, Nygaard IE, Saftlas A, Burns TL, Torner JC, Galask RP
Am J Obstet Gynecol. 2005 Jun;192(6):1829-34

Objective The purpose of this study was to compare the rates of painful bladder syndrome and functional bowel disorders in women with vulvar disease and control subjects. **Study design** In this cross-sectional survey, a questionnaire that contained validated outcome measures was administered to women who were seeking care in a vulvar disease clinic and in general gynecology clinics. **Results** Women who were seen at a vulvar disease clinic were 2.18 (95% CI, 1.19, 3.97) times more likely to have painful bladder syndrome and 2.13 (95% CI, 1.35, 3.35) times more likely to have functional bowel disorders than general gynecology clinic control subjects after multivariable analyses. **Conclusion** Painful bladder syndrome and functional bowel disorders are more prevalent in women who are seen at a vulvar disease clinic than gynecology clinics control subjects. These associations may reflect a common origin for these disorders in certain women. These findings lay the groundwork for future research to investigate a potential "pelvic floor pain disorder," which is a disease entity that would combine the diagnostic criteria for vulvar, bladder, and bowel pain disorders.

Physiotherapy treatment of sexual pain disorders.

Rosenbaum TY
Journal of Sex & Marital Therapy, Vol 31, Number 4, Pgs 329-40

Physiotherapists provide treatment to restore function, improve mobility, relieve pain, and prevent or limit permanent physical disabilities of patients suffering from injuries or disease. Women with vulvar pain, dyspareunia, or vaginismus have limited ability to function sexually and often present with musculoskeletal and neurological findings appropriately addressed by a trained physiotherapist. Although pelvic floor surface electromyography (sEMG) biofeedback has been studied, the inclusion of physiotherapy in the team approach to treating women with sexual pain disorders is a relatively recent advancement, and its exact role is not widely understood by doctors, mental health professionals, or laypersons. This article will examine the supportive and often primary role of the physiotherapist in the overlapping conditions of vaginismus and dyspareunia.

Evaluation of the role of pudendal nerve integrity in female sexual function using noninvasive techniques.

Connell K, Guess MK, La Combe J, Wang A, Powers K, Lazarou G, Mikhail M

Am J Obstet Gynecol. 2005 May;192(5):1712-7

OBJECTIVE: Using quantitative sensory testing and a validated questionnaire, we investigated the role of pudendal nerve integrity in sexual function among women. **STUDY DESIGN:** Participants completed the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ). Vibratory and pressure thresholds were measured at the S2 dermatome reflecting pudendal nerve distribution. **RESULTS:** A total of 56 women enrolled; 29 (51.8%) were asymptomatic and 27 (48.2%) had 1 or more forms of female sexual dysfunction (total sexual dysfunction) including: desire disorder 16.1%, arousal disorder 26.8%, orgasmic disorder 25%, and pain disorder 12.5%. Age, parity, menopausal status, and body mass index were similar between groups. PISQ scores were lower in symptomatic subjects compared with controls ($P < .001$). Decreased tactile sensation was found at the clitoris for women with total sexual dysfunction, desire disorder, and arousal disorder. Women with arousal disorder also had decreased tactile sensation at the perineum. **CONCLUSION:** Pudendal nerve integrity may play a role in female sexual dysfunction.

Nerve stimulator guided pudendal nerve blocks.

Bolandard F, Bazin JE

Can J Anaesth. 2005 Aug;52(7):773

Psychological factors associated with perception of experimental pain in vulvar vestibulitis syndrome.

Granot, M, Lavee, Y

Journal of Sex & Marital Therapy, 31:285-302, 2005

This study assessed the association between pain perception and psychological variables in women with vulvar vestibulitis syndrome (VVS) by comparing 28 VVS women with 50 healthy women. We assessed non genital systemic pain perception with quantitative sensory testing by administering experimental pain stimuli to the forearm. The VVS women demonstrated a lower pain threshold and a higher magnitude estimation of pain, combined with a higher trait anxiety, increased somatization, and a lower body image. Among the VVS women, nonvaginal pain catastrophizing was significantly related to reported pain during coitus. A cluster analysis revealed four subtypes of VVS women, as characterized by levels of pain and personality variables. I suggest implications for the assessment and treatment of women suffering from painful coitus.

Psychological aspects of vulvar vestibulitis syndrome.

Green J, Hetheron J

J Psychosom Obstet Gynaecol. 2005 Jun;26(2):101-6

This review is based on a MEDLINE/PSYCHINFO search for all papers on psychological aspects of vulvar vestibulitis syndrome (VVS) published 1995-2002. VVS is a condition in which painful patches appear on the vulva which make intercourse painful. Causation, natural history and prevalence of VVS are unknown. Attempts to identify psychological characteristics typical of women with VVS have not yielded consistent results with some studies suggesting high levels of psychopathology and others not. It is suggested that inconsistencies in findings reflect not only decisions by women about whether and how to access health care but also the health care system acting to actively filter those reaching specialist services and selecting those with particular psychological characteristics. There is no compelling evidence that VVS per se is associated with any particular psychological or behavioural characteristics other than the sort of difficulties in sexual functioning which might be expected with chronic vulval pain. However there is evidence for high levels of psychological distress in some samples of women with VVS being seen in secondary care.

The vulva and vagina manual.

ISBN 0-646-44531-6

Dennerstein G, Scurry J, Brennan J, Allen D, Marin G
<http://www.gynederm.com.au/>

National institutes of health grant awards for pain, nausea, and dyspnea research: An assessment of funding patterns in 2003.

Bradshaw, DH, Nakamura, Y, Chapman, CR
The Journal of Pain, Vol 6, No 5 (May), 2005: pp 277-293

We introduce an interactive database that permits description and exploration of National Institutes of Health (NIH) funding patterns for research on pain, nausea, and dyspnea. The database encompasses both basic science and clinical research. This article describes how we created the database, including the procedures we developed for reviewing and classifying research grants. In addition, it reports NIH grants and funding activity for the year 2003, with a breakdown of funding activity by Institute and funding comparisons across Institutes. It also describes a first attempt to identify clinically significant but underfunded research domains. In 2003, the NIH funded 1148 grants having relevance to the domain of pain, representing 2.5% of the total NIH research budget. Of those, 581 grants, or about 1% of the NIH budget, had a primary focus on pain. Of the diseases and conditions addressed by the current implementation, musculoskeletal conditions were the best represented with 105 grants, whereas cardiac conditions had the fewest number of grants with 7. The NIH funded 43 grants for dyspnea research and a scant 29 grants for nausea studies. We discuss the current limitations of the database and our plans for further development.

Vulvar Dermatoses

None.

Infectious Disease

None.

Basic Science

Evidence for the innervation of pelvic floor muscles by the pudendal nerve.

Guaderrama NM, Liu J, Nager CW, Pretorius DH, Sheean G, Kassab G, Mittal RK
Obstet Gynecol. 2005 Oct;106(4):774-81

OBJECTIVE: To evaluate whether the pudendal nerve innervates the levator ani muscles by assessing the effect of pudendal nerve blockade on pelvic floor muscle function. **METHODS:** Eleven nulliparous women without symptoms of anal or urinary incontinence were studied before and after pudendal nerve blockade with vaginal manometry, electromyography of the external anal sphincter and puborectalis muscle, and 3-dimensional transperineal ultrasound imaging of the urogenital hiatus during rest and squeeze. **RESULTS:** After pudendal nerve blockade, mean vaginal resting pressures decreased from 19 +/- 10 mm Hg to 15 +/- 10 mm Hg ($P < .05$), and mean vaginal squeeze pressures decreased from 61 +/- 29 mm Hg to 37 +/- 24 mm Hg ($P < .05$). After pudendal nerve blockade, the anterior-posterior length of the urogenital hiatus increased from 51 +/- 4 mm to 55 +/- 5 mm at rest ($P < .05$) and increased from 47 +/- 3 mm to 52 +/- 5 mm during squeeze ($P < .05$). Resting and squeeze electromyography amplitude of the external anal sphincter and puborectalis muscle was markedly reduced by pudendal nerve blockade. **CONCLUSION:** Pudendal nerve blockade decreases vaginal pressures, increases length of urogenital

hiatus, and decreases electromyography activity of the puborectalis muscle, all of which suggest that the pudendal nerve does innervate the levator ani muscle.

Anatomy of the clitoris.

O'Connell HE, Sanjeevan KV, Hutson JM
J Urol. 2005 Oct;174(4 Pt 1):1189-95

PURPOSE: We present a comprehensive account of clitoral anatomy, including its component structures, neurovascular supply, relationship to adjacent structures (the urethra, vagina and vestibular glands, and connective tissue supports), histology and immunohistochemistry. We related recent anatomical findings to the historical literature to determine when data on accurate anatomy became available. **MATERIALS AND METHODS:** An extensive review of the current and historical literature was done. The studies reviewed included dissection and microdissection, magnetic resonance imaging (MRI), 3-dimensional sectional anatomy reconstruction, histology and immunohistochemical studies. **RESULTS:** The clitoris is a multiplanar structure with a broad attachment to the pubic arch and via extensive supporting tissue to the mons pubis and labia. Centrally it is attached to the urethra and vagina. Its components include the erectile bodies (paired bulbs and paired corpora, which are continuous with the crura) and the glans clitoris. The glans is a midline, densely neural, non-erectile structure that is the only external manifestation of the clitoris. All other components are composed of erectile tissue with the composition of the bulbar erectile tissue differing from that of the corpora. The clitoral and perineal neurovascular bundles are large, paired terminations of the pudendal neurovascular bundles. The clitoral neurovascular bundles ascend along the ischiopubic rami to meet each other and pass along the superior surface of the clitoral body supplying the clitoris. The neural trunks pass largely intact into the glans. These nerves are at least 2 mm in diameter even in infancy. The cavernous or autonomic neural anatomy is microscopic and difficult to define consistently. MRI complements dissection studies and clarifies the anatomy. Clitoral pharmacology and histology appears to parallel those of penile tissue, although the clinical impact is vastly different. **CONCLUSIONS:** Typical textbook descriptions of the clitoris lack detail and include inaccuracies. It is impossible to convey clitoral anatomy in a single diagram showing only 1 plane, as is typically provided in textbooks, which reveal it as a flat structure. MRI provides a multiplanar representation of clitoral anatomy in the live state, which is a major advantage, and complements dissection materials. The work of Kobelt in the early 19th century provides a most comprehensive and accurate description of clitoral anatomy, and modern study provides objective images and few novel findings. The bulbs appear to be part of the clitoris. They are spongy in character and in continuity with the other parts of the clitoris. The distal urethra and vagina are intimately related structures, although they are not erectile in character. They form a tissue cluster with the clitoris. This cluster appears to be the locus of female sexual function and orgasm.