

## NVA RESEARCH UPDATE NEWSLETTER

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This newsletter is quarterly and contains abstracts from medical journals published between September and December 2008. Abstracts presented at scientific meetings may also be included. Please direct any comments regarding this newsletter to [chris@nva.org](mailto:chris@nva.org).

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### Vulvodynia/Pain

#### **Assessment of vulvodynia symptoms in a sample of U.S. women: a follow-up national incidence survey.**

Sutton JT, Bachmann GA, Arnold LD, Rhoads GG, Rosen RC  
J Womens Health (Larchmt). 2008 Oct;17(8):1285-92

**OBJECTIVE:** To estimate the annual incidence of vulvodynia-like symptoms and evaluate triggers of vulvar pain in a sample of U.S. women. **METHODS:** After a 1-year interval, women who previously participated in a national vulvodynia prevalence study were recontacted and administered a telephone questionnaire that assessed self-reported vulvodynia-like symptoms and triggers of symptoms. **RESULTS:** From the original cohort of 425 women, 285 (67%) participated in this follow-up study. Symptoms consistent with vulvodynia occurring within 1 year of initial contact were reported by 4.7% of previously asymptomatic women. Nearly 50% of the original patients again reported a history of vulvodynia-like symptoms, with 68.6% of these as persistent over the past year. Of significance, pain or discomfort with first-time tampon use was 2.15 times more likely (95% CI 1.0-4.62) in symptomatic women. These women were also 2.4 times more likely (95% CI 1.29-4.53) to use a combination of tampons and pads for sanitary protection rather than one method alone. **CONCLUSIONS:** Over the course of 1 year, as many as 1 in 20 women may experience new-onset chronic genital pain. Despite a higher likelihood of having discomfort or pain with first tampon use, symptomatic women did not exhibit a preference for sanitary napkins. This indicates that lack of tampon use because of pain may not be an effective screening criterion for vulvodynia. We recommend additional studies with symptomatic and diagnosed women to explore in more detail the issues surrounding tampon use history and chronic genital pain.

#### **Vulvodynia in preadolescent girls.**

Reed BD, Cantor LE  
J Low Genit Tract Dis. 2008 Oct;12(4):257-61

**OBJECTIVE:** Although vulvodynia occurs in approximately 7% of adult American women, we hypothesize that vulvodynia also occurs in young girls and that they respond to treatments that are similar to those used in women with this disorder. **MATERIALS AND METHODS:** This is a retrospective case study of vulvodynia in preadolescent girls seen in our referral practice. Records of all office visits and any telephone or e-mailed follow-up were reviewed. **RESULTS:** Between October 1996 and April 2006, 6 girls ages 4 to 11 years were evaluated and diagnosed with vulvodynia. Pain had been present for several

months to 7 years, and most patients had been seen by several physicians before having this diagnosis made. Treatment was typically initiated with a tricyclic antidepressant, and 5 of the 6 girls noted improvement in their symptoms, including 2 who had marked improvement, and another 3 with substantial improvement who were able to discontinue therapy without a recurrence. **CONCLUSIONS:** Vulvodynia does occur among young girls and, when treated as a neuropathic pain disorder, was found to dramatically improve or remit in the majority of those treated in this small case series. This underrecognized disorder should be considered in cases of ongoing vulvar discomfort, regardless of age.

#### **A population-based study of dyspareunia in a cohort of middle-aged Brazilian women.**

Valadares AL, Pinto-Neto AM, Conde DM, Sousa, MH, Osis MJ, Costa-Paiva L  
Menopause. 2008 Nov-Dec;15(6):1184-90

**OBJECTIVE:** To investigate the prevalence of dyspareunia and its associated factors in a cohort of middle-aged women. **DESIGN:** A cross-sectional, population-based study was carried out using an anonymous, self-report questionnaire completed by 200 Brazilian-born women, 40 to 65 years of age, with 11 years or more of formal education. The evaluation instrument was based on the Short Personal Experiences Questionnaire. Sociodemographic, clinical, behavioral, reproductive, and partner-related factors were assessed. Poisson multiple regression analysis was performed, and prevalence ratios (PRs) with their 95% CIs were calculated. **RESULTS:** The prevalence of dyspareunia was 39.5%. Multiple analysis showed that dyspareunia was more common in women who reported nervousness (PR = 1.73, 95% CI: 1.14-2.63) and depression (PR = 1.69, 95% CI: 1.09-2.61). A score of more than 3 for frequency of sexual activity (PR = 0.20, 95% CI: 0.05-0.84) and having had more than two pregnancies (PR = 0.62, 95% CI: 0.48-0.81) were factors indicative of a protective effect against dyspareunia. **CONCLUSIONS:** Dyspareunia was common in this cohort of middle-aged women. Nervousness and depression increased the likelihood of experiencing dyspareunia. These findings suggest that psychological symptoms should be taken into consideration in the management of the middle-aged woman with dyspareunia, and measures should be adopted to minimize the repercussions of these factors on sexuality.

#### **A German survey of subjective gynaecological complaints.**

Weidner K, Richter J, Bittner A, Winter UM, Stobel-Richter Y, Brahler E  
Psychother Psychosom Med Psychol. 2008 Sep 15. [Epub ahead of print]

This report encompasses a representative survey of the German feminine population. The aim of this survey is to assess subjective gynaecological complaints. These were registered by the newly constructed "Giessen Subjective Complaints List - for women". This questionnaire measures specific gynaecological complaints of several body areas (excretion, pelvic pain, breast, vulva, menses). Participants included n = 1 093 women between the age of 14 and 77 years. The highest complaint rates of the study participants were observed in the area of menstrual symptoms. Overall, 31 % (n = 206) of the surveyed women indicated that they suffered somewhat, extensively, or highly from menstrual complaints (e. g. painful menstruation or menorrhagia). These menstrual symptoms were significantly higher in younger women (14-45 yr.). Symptoms of other complaint areas (excretion, e. g. urinary incontinence; breast, e. g. sensitivity) were slightly less dominant than menstrual symptoms with 17 % (n = 186) and 13 % (n = 128) respectively. It was shown that subjective gynaecological complaints show a typical age-dependent developmental course. They represent the major psychosocial topic of the current phase of life for each woman. This study is a contribution to the epidemiology of subjective gynaecological complaints in the German feminine population.

#### **Sexual problems and distress in United States women: prevalence and correlates.**

Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB  
Obstet Gynecol 2008;112 970-978

**OBJECTIVE:** To estimate the prevalence of self-reported sexual problems (any, desire, arousal, and orgasm), the prevalence of problems accompanied by personal distress, and to describe related

correlates. METHODS: The 31,581 female respondents aged 18 years and older were from 50,002 households sampled from a national research panel representative of U.S. women. Correlates of each distressing sexual problem were evaluated using multiple logistic regression techniques. RESULTS: The age-adjusted point prevalence of any sexual problem was 43.1% and 22.2% for sexually related personal distress (defined as a score of at least 15 on Female Sexual Distress Scale). Any distressing sexual problem (defined as reporting both a sexual problem and sexually related personal distress, Female Sexual Distress Scale score of at least 15) occurred in 12.0% of respondents and was more common in women aged 45-64 years (14.8%) than in younger (10.8%) or older (8.9%) women. Correlates of distressing sexual problems included poor self-assessed health, low education level, depression, anxiety, thyroid conditions, and urinary incontinence. CONCLUSION: The prevalence of distressing sexual problems peaked in middle-aged women and was considerably lower than the prevalence of sexual problems. This underlines the importance of assessing the prevalence of sexually related personal distress in accurately estimating the prevalence of sexual problems that may require clinical intervention. LEVEL OF EVIDENCE: III.

### **Sexual dysfunction prevalence rates: marketing or real?**

Nygaard I

*Obstet Gynecol.* 2008; 112: 968-969

No abstract available.

### **Trends in funding for research on pain: a report on the National Institutes of Health grant awards over the years 2003 to 2007.**

Bradshaw DH, Empy C, Davis P, Lipschitz D, Nakamura Y, Chapman CR

*The Journal of Pain.* Vol 9. Issue 12, Dec 2008, Pages 1077-1087.e8

In recent years, the National Institutes of Health (NIH) has experienced unprecedented reductions in its customary annual budget increases. Consequently, researchers, health care policy planners and others have a pressing need for accurate information on NIH funding patterns. We created a unique and objective system for compiling, classifying, and analyzing data on NIH grant awards and funding for research on pain, nausea, and dyspnea using naïve observers, cross-validation by multiple raters, and face validation by experts. We present results of our method and analyses for the period from 2003 to 2007. Following a 12% increase from 2003 to 2004, funding for pain research fell by 9.4% per year on average over the next 3 years. The percent of the total NIH budget going to support pain research increased to 0.78% in 2004 but fell to 0.61% in 2007. A piecewise regression model confirmed the declining trend represented a significant fit to the data ( $R^2=0.98$ ,  $p=0.024$ ). Separate breakdowns by Institutes showed similar patterns. Analyses of nausea and dyspnea research support revealed small but steady increases over the same period. Declining support for pain research disproportionate to decreases in the NIH budget signals a need for measures to promote funding for meritorious applications.

### **Addressing the decline in NIH pain research funding.**

Max MB

*The Journal of Pain.* Vol 9, Issue 12, Dec 2008, Pages 1074-1076

No abstract available.

### **The healthcare bubble through the lens of pain research, practice, and policy: advice for the new president and congress.**

Green CR

*The Journal of Pain.* Vol 9, Issue 12, Dec 2008, Pages 1071-1073

No abstract available.

### **Increased gray matter density in young women with chronic vulvar pain.**

Schweinhardt P, Kuchinad A, Pukall CF, Bushnell MC  
Pain. 2008 Dec;140(3):411-419

Provoked vestibulodynia (PVD) is a common form of chronic vulvar pain with unknown aetiology. Central pain regulatory mechanisms have been suggested to be disrupted in PVD, and consequently, PVD may be associated with anatomical changes in pain modulatory brain areas. Here, we compared total gray matter volumes and regional gray matter densities between 14 medication-free young women with relatively short-standing PVD (1 to 9 yrs) and 14 control subjects using whole brain voxel-based morphometry (VBM). VBM revealed that PVD subjects had significantly higher gray matter densities in pain modulatory and stress-related areas, i.e. the parahippocampal gyrus/hippocampus and basal ganglia (globus pallidus, caudate nucleus, and substantia nigra). In several of these regions, gray matter was related to clinical symptoms, namely lowered pain thresholds and increased pain catastrophizing scores. No region showed decreased gray matter density in the PVD group. These results point at the morphological alterations in supra-spinal pain modulatory circuitry, which might contribute to the clinical symptoms of patients with PVD. Previous VBM studies in older subjects with a longstanding chronic pain condition have demonstrated gray matter decreases in similar areas. We therefore speculate that gray matter density might increase in young pain patients with short disease duration and decrease in older subjects with longstanding disease, similarly to some psychiatric conditions, in which bi-directional changes of gray matter have been observed.

### **Pain, psychosocial, sexual, and psychophysical characteristics of women with primary vs. secondary provoked vestibulodynia.**

Sutton KS, Pukall CF, Chamberlain S  
Journal of Sexual Medicine. Published Online: Oct 30, 2008.

**Introduction.** Women with provoked vestibulodynia (PVD), a common cause of dyspareunia, are typically considered a homogeneous group. However, research suggests that differences on some factors (e.g., medical history, pain characteristics, psychological functioning, treatment response) exist based upon whether the pain was present at first intercourse (primary PVD: PVD1) or developed at some later point (secondary PVD: PVD2).

**Aims.** The purpose of this study was to examine differences in demographic variables, pain characteristics, psychosocial and psychosexual adjustment, and pain sensitivity between women with PVD1 and PVD2. **Methods.** Twenty-six women suffering from PVD (13 with PVD1 and 13 with PVD2) completed a screening assessment, a standardized gynecological examination, an interview, questionnaires, and a quantitative sensory testing session.

**Main Outcome Measures.** These included pain ratings during the gynecological examination and interview, scores on measures of psychosocial/sexual functioning (e.g., Short Form-36 [SF-36] Health Survey, Female Sexual Function Index), and thresholds and pain ratings during thermal sensory testing over the dominant forearm and vulvar vestibule. **Results.** The women with PVD1 were more likely to be nulliparous, but they were not significantly different from the women with PVD2 on other demographic variables or in their pain ratings during the gynecological examination. The women with PVD1 reported lower levels of social and emotional functioning and heightened anxiety surrounding body exposure during sexual activity, and they also displayed lower heat pain tolerance over the forearm and lower heat detection and pain thresholds at the vulvar vestibule than the women with PVD2. **Conclusions.** The findings from this study support previous research indicating that women with PVD1 and PVD2 differ in a number of domains. Further research is needed to confirm and elaborate on these findings.

### **A survey on diagnosis and treatment of vulvodynia among vulvodynia researchers and members of the International Society for the Study of Vulvovaginal Disease.**

Reed BD, Haefner HK, Edwards L  
J Reprod Med 2008;53:921-929

**OBJECTIVE:** To survey members of the International Society for the Study of Vulvovaginal Disease and authors of recent related medical publications for whom e-mail addresses were available to assess current opinion and practices. **STUDY DESIGN:** In a cross-sectional online survey of potential participants, characteristics of respondents and their preferred diagnostic criteria and treatment modalities for vulvodynia were assessed using univariate and multivariate methods. **RESULTS:** Of recipients, 61.0% completed the survey. Of these, 86.7% were active in diagnosing or treating women with vulvodynia and 41.3% were currently active in vulvodynia research. Of respondents, >80% include a history, a genital visual examination and vulvar pressure sensitivity testing in their evaluation of women with vulvar pain. Laboratory assessments were less likely to be rated essential or helpful. Of participants, >80% rated as very effective or somewhat effective tricyclic antidepressants, pelvic floor physical therapy and psychologic counseling. Most indicated they have made the diagnosis of vulvodynia in conjunction with other vulvovaginal diagnoses and agreed that vulvodynia does remit for some women. **CONCLUSION:** Despite many diagnostic and treatment options available, some consensus on diagnostic and treatment preferences for vulvodynia was identified. Further research to develop the evidence base for diagnostic and treatment decisions is needed.

### **Vulvodynia. Definition, diagnosis and treatment.**

Petersen CD, Lundvall L, Kristensen E, Giraldi A  
Acta Obstet Gynecol Scand. 2008;87(9):893-901

Vulvodynia is a chronic painful disorder with an estimated prevalence of 9-12%. A rising incidence of the condition constitutes a growing problem. This has led to an increased focus on etiology and treatment, while the definition also requires attention. Previous assumptions stating that the problem is solely a psychological disorder have been abandoned, because inflammatory mechanisms and genetic factors have been found to be involved in the pathogenesis as well as psychosexual contributors. This article describes the terminology and definition of the condition, theories on patho-physiological mechanisms underlying the disorder, methods of diagnosis and evidence and recommendations on clinical management. A critical examination of the literature regarding vulvodynia reveals numerous strategies and recommendations for treatment, many of which are not evidence-based, and a lack of effective treatment for all patients. Research is being undertaken internationally to find more specific and unequivocal causes of the disorder, as well as to develop evidence-based methods of treatment.

### **Topical gabapentin in the treatment of localized and generalized vulvodynia.**

Boardman LA, Cooper AS, Blais LR, Raker CA  
Obstet Gynecol. 2008 Sep;112(3):579-85

**OBJECTIVE:** To evaluate the clinical efficacy and tolerability of topical gabapentin in the treatment of women with vulvodynia. **METHODS:** A retrospective study was designed to ascertain clinical responses to topical gabapentin. Patient demographic and medical characteristics, including present and prior treatment for vulvodynia, were routinely collected. The final outcome was defined by a comparison between pretreatment and posttreatment mean pain scores based on a discrete visual analog scale of 0 to 10. Categorical data were compared by Fisher exact test, continuous variables between groups by the Wilcoxon rank sum test, and mean change in pain score between pretreatment and posttreatment by paired Student t test. **RESULTS:** Between January 2001 and December 2006, 51 women with vulvodynia (19 or 37% with generalized vulvodynia, 32 or 63% with localized) were treated with 2% to 6% gabapentin. After a minimum of 8 weeks of therapy, the mean pain score among the 35 evaluable women was significantly reduced from 7.26 to 2.49 (mean change -4.77, 95% confidence interval -5.47 to -4.07). Overall, 28 of 35 (80%) demonstrated at least a 50% improvement in pain scores. Among patients with localized vulvodynia, sexual function improved in 17 of 20 with evaluable results (6 of 9 reinstated vaginal intercourse, whereas all 11 patients experiencing decreased frequency of intercourse reported increased frequency after treatment). Discontinuations occurred in 7 of 50 (14%) treated. **CONCLUSION:** Topical gabapentin seems to be well-tolerated and associated with significant pain relief in women with vulvodynia. **LEVEL OF EVIDENCE:** III.

**Use of transcutaneous electrical stimulation and biofeedback for the treatment of vulvodynia (vulvar vestibular syndrome): result of 3 years of experience.**

Dionisi B, Anglana F, Inghirami P, Lippa P, Senatori R  
Minerva Ginecol. 2008 Dec;60(6):485-491

AIM: The safety, tolerability and efficacy of physical therapy with biofeedback and trans electrical nerve stimulation (TENS) with intravaginal probe for the treatment of vulvar pain and vulvar discomfort in women with vulvodynia, is evaluated in the present study. Vulvodynia is a chronic syndrome of unexplained vulvar pain. Patients typically present with a history of intermittent or continuous, localized, vulvar pain, frequently accompanied by sexual dysfunction like entry dyspareunia, burning and itching localized to the vulvar vestibule. METHODS: From January 2005 and June 2007, a total 145 women diagnosed with vulvodynia presented in the ambulatory for the Diagnosis and Treatment of Vulvar Pain and Pelvic Floor Dysfunction, Clinical "Santa Famiglia", Rome. Patients were treated with weekly biofeedback (BFB) and transcutaneous electroanalgesia (TENS), in association with functional electrical stimulation (FES) and home-therapy with stretching exercise of pelvic floor. RESULTS: Hundred forty-five women completed both the biofeedback and trans electric nerve stimulation treatment for a total of 10 application, with a improvement of vulvar pain in 75.8% of cases. CONCLUSION: The pelvic floor relaxation with biofeedback and electroanalgesia is safe and effective in improvement in vulvar pain and dyspareunia in women with vulvodynia.

**Combined physical and psychosexual therapy for provoked vestibulodynia-an evaluation of a multidisciplinary treatment model.**

Backman H, Widenbrant M, Bohm-Starke N, Dahlof LG  
J Sex Res. 2008 Oct-Dec;45(4):378-85

Our objective is to standardize and evaluate a combined physical and psychosexual therapy for women with provoked vestibulodynia. Twenty-four patients underwent the treatment program. Sessions with a psychosexual counselor included issues on sexual functioning, psychological adjustments, and stress elimination. Exercises for mucosal desensitization and reestablishment of pelvic floor function were supervised by a midwife. A questionnaire was used for evaluation at a minimum of 6 months after the treatment. The mean number of appointments to the counselor was 12 (4-24) and 15 (9-26) to the midwife during a mean period of 53 weeks (19-92). Nineteen women (79%) considered themselves to be cured or having greatly improved. Intercourse frequency was increased ( $p = 0.001$ ) and coital pain was reduced ( $p = 0.02$ ) after completing the treatment. Improvements in sexual functioning and coping strategies for psychological impairment and stress were reported. Women with provoked vestibulodynia benefit from a multidisciplinary treatment model including desensitization of the vestibular mucosa, rehabilitation of the pelvic floor, and psychosexual adjustments.

**A randomized clinical trial for women with vulvodynia: cognitive-behavioral therapy vs. supportive psychotherapy.**

Masheb RM, Kerns RD, Lozano C, Minkin MJ, Richman S  
Pain. 2008 Nov 18. [Epub ahead of print]

Many treatments used for women with vulvodynia are based solely upon expert opinion. This randomized trial aimed to test the relative efficacy of cognitive-behavioral therapy (CBT) and supportive psychotherapy (SPT) in women with vulvodynia. Of the 50 participants, 42 (84%) completed 10-week treatments and 47 (94%) completed one-year follow-up assessments. Mixed effects modeling was used to make use of all available data. Participants had statistically significant decreases in pain severity ( $p's < 0.001$ ) with 42% of the overall sample achieving clinical improvement. CBT, relative to SPT, resulted in significantly greater improvement in pain severity during physician examination ( $p = 0.014$ ), and greater improvement in sexual function ( $p = 0.034$ ), from pre- to post-treatment. Treatment effects were well maintained at one-year follow-up in both groups. Participants in the CBT condition reported significantly greater treatment improvement, satisfaction and credibility than participants in the SPT condition ( $p's < 0.05$ ). Findings from the present study suggest that psychosocial treatments for vulvodynia are

effective. CBT, a directed treatment approach that involves learning and practice of specific pain-relevant coping and self-management skills, yielded better outcomes and greater patient satisfaction than a less directive approach.

### **Does the Prolift system cause dyspareunia?**

Lowman JK, Jones LA, Woodman PJ, Hale DS  
Am J Obstet Gynecol. 2008 Oct 31. [Epub ahead of print]

**OBJECTIVE:** The purpose of this study was to determine the de novo dyspareunia rate with the Prolift procedure. **STUDY DESIGN:** All Prolift cases performed between August 2005 and August 2007 were evaluated. The rate of de novo dyspareunia was calculated by chart review. Type and degree of dyspareunia were assessed by self-administered questionnaire. Demographics, use of hormone therapy, failure rate, and willingness to have the surgery again were summarized using descriptive statistics. **RESULTS:** The rate of de novo dyspareunia was 16.7%. Over 75% of patients with de novo dyspareunia described the pain as mild or moderate. Most described dyspareunia with insertion. Eighty-three percent of respondents with de novo dyspareunia would have the procedure done again. **CONCLUSION:** The Prolift is associated with a 17% de novo dyspareunia rate. Despite this, most would have the surgery done again.

### **Post-coital burning pain and pain at micturition: early symptoms of partial vaginismus with or without vulvar vestibulitis?**

Engman M, Wijma K, Wijma B  
J Sex Marital Ther. 2008;34(5):413-28

Twenty-four women with partial vaginismus with or without vulvar vestibulitis participated in a semi-structured telephone interview concerning early signs and development of their pain symptoms during/after intercourse. At the onset of the problem, pain after intercourse was more common than pain during penetration. Pain intensity during penetration increased from the onset of the problem to when the women ceased having intercourse. Pain during penetration lasted for 1 minute, and was most often described as sharp/incisive/bursting, while pain after intercourse had a duration of 2 hours and was described as burning and/or smarting. Post-coital pain during micturition was described by 70% of the women.

### **Antecedent nonbladder syndromes in case-control study of interstitial cystitis/painful bladder syndrome.**

Warren JW, Howard FM, Cross RK, Good JL, Weissman MM, Wessermann U, Langenberg P, Greenberg P, Clauw DJ  
Urology. 2008 Nov 7. [Epub ahead of print]

**OBJECTIVES:** Probing for clues to the pathogenesis of interstitial cystitis/painful bladder syndrome (IC/PBS), we sought antecedent nonbladder syndromes that distinguished incident IC/PBS cases from matched controls. **METHODS:** Female incident IC/PBS cases were recruited nationally, and their IC/PBS onset date (index date) was established. The controls were recruited by national random digit dialing and matched to the cases by sex, age, region, and interval between the (assigned) index date and interview. The prevalence of 24 nonbladder syndromes before the index date was assessed, 7 by multiple methods. **RESULTS:** The cases with IC/PBS had greater antecedent prevalence of 11 syndromes, and 243 of 313 cases (78%) vs 145 of 313 controls (45%) had multiple syndromes ( $P < .001$ ). Fibromyalgia-chronic widespread pain (FM-CWP), chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome were associated with each other by pairwise and factor analyses using numerous assumptions. Cases with FM-CWP, chronic fatigue syndrome, sicca syndrome, and/or irritable bowel syndrome ( $n = 141$ , 45%) were more likely to have other syndromes (ie, migraine, chronic pelvic pain, depression, and allergy). Three other syndrome clusters were identified; each was associated with this FM-CWP cluster. **CONCLUSIONS:** Eleven antecedent syndromes were more often diagnosed in those with IC/PBS, and

most syndromes appeared in clusters. The most prominent cluster comprised FM-CWP, chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome; most of the other syndromes and identified clusters were associated with it. Among the hypotheses generated was that some patients with IC/PBS have a systemic syndrome and not one confined to the bladder.

### **Vulvodynia & pelvic pain? Think interstitial cystitis.**

Siegel JR, Sand PK, Sasso K  
Nurse Pract. 2008 Oct;33(10):40-5

No abstract available.

### **Effects of vulvodynia on quality of life.**

Ponte M, Klemperer E, Sahay A, Chren MM  
J Am Acad Dermatol. 2008 Nov 18. [Epub ahead of print]

**BACKGROUND:** The experiences of women with vulvodynia are poorly understood. **OBJECTIVE:** We sought to determine the effects of vulvodynia on quality of life. **METHODS:** We conducted a survey of 280 patients in a university-based vulvar disorders clinic. Skin-related quality of life was measured with a vulvar-specific version of Skindex-29. **RESULTS:** The response rate was 95%; 101 patients (36%) had vulvodynia, and 179 patients (64%) had other vulvar conditions. Women with vulvodynia had significantly worse quality of life than patients with many other dermatologic conditions, and worse functioning than women with other vulvar conditions (mean functioning scores [ $\pm$ SD] of patients with psoriasis, other vulvar conditions, and vulvodynia were 23  $\pm$  27, 34  $\pm$  24, and 44  $\pm$  22, respectively,  $P = .05$ ). A diagnosis of vulvodynia was the strongest independent correlate of poor quality of life (eg, for poor functioning, odds ratio = 1.8, 95% confidence interval 1.0-3.1). **LIMITATIONS:** Limitations are single academic medical center and comorbid illnesses determined by self-report. **CONCLUSION:** Vulvodynia has broad and substantial effects on quality of life.

## **Other Vulvovaginal Disorders**

### **Comparison of vulvar skin diseases in black and white women: a histopathological study.**

Puggina J, Andrade LA, Souza EM, Cintra ML  
J Eur Acad Dermatol Venereol. 2008 Nov;22(11):1391-2

No abstract available.

### **Postmenopausal vulval disease.**

Olsson A, Selva-Nayagam P, Oehler MK  
Menopause Int. 2008 Dec;14(4):169-72

Vulval disease in the postmenopausal age group is relatively common. Some vulval conditions such as lichen sclerosus are more prevalent in the postmenopausal years. Often more than one condition is present at the same time. Accurate diagnosis is essential for effective treatment. The risk of progression to malignancy associated with some of these diseases dictates long-term surveillance.

### **Cytology in the differential diagnosis of vaginitis.**

Dennerstein GJ  
Curr Infect Dis Rep. 2008 Nov;10(6):485-9



Vaginal discharge, vulvar pruritus, and dyspareunia are among the most common symptoms that prompt women to seek medical advice. They are frequently assumed to be due to vaginitis resulting from infection and are treated with anti-infective agents without further investigation. Such empirical treatment may be successful, but on the frequent occasions when such treatment is inappropriate, the stage is set for deteriorating genital health. I believe that most cases of "vulvodynia" could be prevented by a correct diagnosis and treatment at the onset of symptoms.

#### **Vulvovaginal candidiasis and bacterial vaginosis.**

Nyirjesy P

Infect Dis Clin North Am. 2008 Dec;22(4):637-52

Vulvovaginal candidiasis (VVC) and bacterial vaginosis (BV) are frequently encountered in clinical practice. Recent advances have furthered understanding of pathophysiology. Proper diagnosis, based on appropriate office and, in complicated cases, laboratory tests is the key to rational selection of therapy. For women who have routine uncomplicated episodes of VVC or BV, a variety of effective treatment options exists. Recurrent disease remains a challenge for these conditions but can often be managed successfully.

#### **First molecular method for discriminating between *Candida africana*, *Candida albicans*, and *Candida dubliniensis* by using hwp1 gene.**

Romeo O, Criseo G

Diagn Microbiol Infect Dis. 2008 Oct;62(2):230-3

The authors report here a polymerase chain reaction-based assay using a single primer pair (CR-f/CR-r), allowing discrimination between *Candida africana* and *Candida albicans* by using the hwp1 gene. The method also identifies *Candida dubliniensis* because it produces 3 different DNA fragments: approximately 700 bp for *C. africana*, 941 bp for *C. albicans*, and 569 for *C. dubliniensis*.

#### **Individualized decreasing-dose maintenance fluconazole regimen for recurrent vulvovaginal candidiasis (ReCiDiF trial).**

Donders G, Bellen G, Byttebier G, Verguts L, Hinoul P, Walckiers R, Stalpaert M, Vereecken A, Van Eldere J

Am J Obstet Gynecol. 2008 Oct 29. [Epub ahead of print]

**OBJECTIVE:** Although many women with recurrent vulvovaginal candidiasis initially benefit from prophylactic intermittent treatment with antimycotics, most of them experience relapse after cessation of therapy, and often they return to the pretreatment recurrence rate. The purpose of this study was to demonstrate the efficacy and safety of an individualized, degressive, prophylactic regimen in 136 women with recurrent vulvovaginal candidiasis. **STUDY DESIGN:** After an induction dose of 600 mg fluconazole during the first week, 117 women started maintenance therapy: 200 mg fluconazole weekly for 2 months, followed by 200 mg biweekly for 4 months, and 200 mg monthly for 6 months, according to their individual response to therapy. All women were tested for recurrences monthly with wet mount microscopy and vaginal culture during the first 6 months and bimonthly during the next 6 months. Patients were allowed to move on to the next level of maintenance therapy only if they were symptom free and microscopy and culture negative. **RESULTS:** Of the women who were cured successfully after the induction phase, 101 women (90%) were disease-free after 6 months of maintenance therapy with this degressive regimen, and 80 women (77%) were disease-free after 1 year. The weekly incidence of the first clinical relapse was 0.5% during any period of the maintenance phase, and the rate of all new relapses, which included evidence of mycologic or microscopic colonization, was 1% per week. Women who experienced several relapses (poor responders) had experienced more relapses before entering the study compared with the optimal responders (odds ratio, 4.9; 95% CI, 1.8-13.7;  $P = .002$ ), experienced the disease for a longer period of time (6.5 vs 3.7 years;  $P = .06$ ), and harbored significantly more *Candida non-albicans* during

maintenance therapy ( $P = .001$ ). No serious side-effects were noted. **CONCLUSION:** Individualized, degressive, prophylactic maintenance therapy with oral fluconazole is an efficient treatment regimen to prevent clinical relapses in women with recurrent vulvovaginal candidiasis.

### **Effective treatment of vaginal atrophy with an ultra-low-dose estradiol vaginal tablet.**

Simon J, Nachtigall L, Gut R, Lang E, Archer DF, Utian W  
Obstet Gynecol 2008;112 1053-1060

**OBJECTIVE:** To evaluate the efficacy of ultra-low-dose 10-microgram 17beta-estradiol (E2) vaginal tablets for treatment of vaginal atrophy. **METHODS:** Postmenopausal women ( $N=309$ ) were randomly assigned to 10-microgram E2 or placebo vaginal tablets for 52 weeks in a multicenter, double-blind study. Primary efficacy endpoints included change from baseline to week 12 in vaginal cytology, vaginal pH, and most bothersome urogenital symptoms score. Grading of vaginal health was a secondary efficacy assessment. Safety assessments included endometrial biopsy, physical and gynecologic examinations, and recording adverse events. **RESULTS:** At week 12, the change from baseline for 10 micrograms E2 compared with placebo demonstrated significant improvement in vaginal Maturation Index (proportion of parabasal cells: -37% compared with -9%; superficial cells: 13% compared with 4%; intermediate cells: 24% compared with 5%;  $P<.001$  for each), Maturation Value (25.0 compared with 6.5,  $P<.001$ ), grading of vaginal health (-0.91 compared with -0.51,  $P<.001$ ), vaginal pH grade (-1.3 compared with -0.4,  $P<.001$ ), and most bothersome symptoms score (-1.23 compared with -0.87,  $P=.003$ ). For each component of vaginal Maturation Index, vaginal Maturation Value, grading of vaginal health, and vaginal pH, treatment effects were statistically different from placebo after 2 weeks of treatment. For most bothersome symptoms, treatment effect became apparent after 4 weeks and reached statistical significance at week 8 of therapy. All treatment effects were statistically significant at week 52. There were no major safety findings regarding physical, gynecologic, or laboratory assessments. **CONCLUSION:** After 12 weeks of treatment, an ultra-low-dose 10-microgram E2 vaginal tablet, compared with placebo, demonstrated significant improvement for the primary endpoints: vaginal cytology and pH and most bothersome urogenital symptoms score. **CLINICAL TRIAL REGISTRATION:** ClinicalTrials.gov, <http://clinicaltrials.gov>, NCT00108849 **LEVEL OF EVIDENCE:** I.

### **The association of lichen sclerosus and erosive lichen planus of the vulva with autoimmune disease: a case-control study.**

Cooper SM, Ali I, Baldo M, Wojnarowska F  
Arch Dermatol. 2008 Nov;144(11):1432-5

**OBJECTIVE:** To investigate the prevalence of autoimmune disease and circulating autoantibodies in women with lichen sclerosus (LS) and erosive lichen planus (LP) of the vulva and to compare these with a control population. **DESIGN:** Age- and sex-matched controlled study. **SETTING:** The vulval clinics in Oxfordshire, England, for patients with LS and LP. Healthy controls were recruited from the hospital and community. **PATIENTS:** A total of 190 women with the typical features of adult-onset LS of the vulva, 126 women with adult-onset erosive LP of the vulva, and 922 female controls (of whom 230 were examined). **INTERVENTIONS:** Personal history of autoimmune disorder for patients and controls, family history of autoimmune disorder for vulval LS and LP cohorts, and an autoantibody screen. **MAIN OUTCOME MEASURES:** The presence or absence of a personal or family history of autoimmune disorder, and the presence or absence of 1 or more circulating autoantibodies. **RESULTS:** The mean ages of patients with LS, patients with erosive LP, and control patients were 63, 61, and 61 years, respectively. The mean age of the 230 controls examined (including those who had serum autoantibodies assayed) was 62 years. Autoimmune disorders were more frequent in patients with erosive LP compared with controls (29% vs 9%;  $P < .001$ ) and in those with LS compared with controls (28% vs 9%;  $P < .001$ ). Circulating autoantibodies were more frequent in those with erosive LP compared with controls (41% vs 20%;  $P < .001$ ). **Conclusion** This study demonstrates an association of autoimmune disorder and autoantibodies with erosive LP of the vulva and confirms the autoimmune associations of vulval LS.

### **Ultraviolet A phototherapy for sclerotic skin diseases: a systematic review.**

Kroft EB, Berkhof NJ, van de Kerhof PC, Gerritsen RM, de Jong EM  
J Am Acad Dermatol. 2008 Dec;59(6):1017-30

**BACKGROUND:** Ultraviolet (UV) A-1 phototherapy is now available for a variety of skin diseases. Increasingly since 1995, there have been investigations of the efficacy of UVA-1 (340-400 nm) therapy for sclerotic skin diseases. Most studies undertaken treated patients who had localized scleroderma, but UVA-1 phototherapy is currently also used for other sclerotic skin conditions. **OBJECTIVE:** We sought to assess the efficacy, biological effects, and side effects of UVA-1 in a variety of sclerotic skin diseases (localized scleroderma, eosinophilic fasciitis, chronic graft-versus-host disease, lichen sclerosus et atrophicus, scleredema adultorum, necrobiosis lipoidica, POEMS disease, pansclerotic porphyria cutanea tarda, and drug-induced scleroderma-like disorders). **METHODS:** The authors searched for publications dated between January 1996 and November 2007 in the computerized bibliographic database, PubMed. PubMed was searched using medical subject heading terms and open searches to retrieve the latest reports. **RESULTS:** The evidence based on research concerning the effect of full-spectrum UVA (320-400 nm) and UVA-1 on these skin diseases is still growing, and appears promising. Up until now, good results are shown for all different doses (low, medium, and high) UVA-1 and UVA. There are insufficient data regarding use of high-dose UVA-1 and there are no comparative studies to make a clear assessment regarding the superiority of low-, medium-, or high-dose UVA-1 therapy. Although UVA-1 has various effects on, for instance, fibroblasts and inflammatory cells, the precise mode of action remains obscure. The main short-term side effects of UVA-1 therapy are erythema, pruritus, xerosis cutis, tanning, and recrudescence of herpes simplex infection. More studies are warranted to investigate the potential long-term risk of photoaging and skin cancer. Currently, UVA-1 is considered to be less carcinogenic than psoralen plus UVA (PUVA). **LIMITATIONS:** Because of the limited availability of randomized controlled trials and large cohort studies, it is difficult to draw firm conclusions on the long-term efficacy, optimum dose, and best treatment regimens for UVA-1 when administered to patients with sclerosing skin disorders. **CONCLUSIONS:** Full-spectrum UVA and UVA-1 phototherapy seem effective in the treatment of sclerotic skin diseases based on data retrieved from the literature. UVA-1 treatment can shorten the active period of localized scleroderma and pseudoscleroderma and prevent further disease progression, including contractures. Further investigations will be needed to determine any additional biological effects of UVA-1. Although long-term side effects are not yet known, UVA-1 might develop into a promising beneficial and well-tolerated treatment in the therapeutic armamentarium for sclerotic skin diseases. Long-term studies in large groups of patients are clearly needed.

### **An open trial of 5-aminolevulinic acid photodynamic therapy for vulvar lichen sclerosus.**

Sotiriou E, Panagiotidou D, Ioannidis D  
Eur J Obstet Gynecol Reprod Biol. 2008 Dec;141(2):187-8

No abstract available.

### **Anogenital allergic contact dermatitis, the role of spices and flavour allergy.**

Vermaat H, Smienk F, Rustemeyer T, Brynzeel DP, Kirtschig G  
Contact Dermatitis. 2008 Oct;59(4):233-7

**BACKGROUND:** In patients with vulval or anogenital dermatitis, irritant contact dermatitis is more common than allergic contact dermatitis. The reported frequency and relevance of contact sensitivity in anogenital dermatitis varies greatly. **OBJECTIVE:** To determine the frequency and relevance of contact sensitization in a Dutch group of female patients with chronic anogenital complaints. **METHODS:** We reviewed patch test results of 53 women with chronic anogenital complaints, with sole vulval symptoms in 29 women and sole perianal in 5, in whom inflammatory skin diseases like lichen sclerosus, lichen planus, psoriasis, as well as infectious diseases were unlikely or excluded as a cause of their symptoms. All women were tested with the European baseline series plus additional test series according to their personal history. **RESULTS:** Thirty-five patients (66%) showed one or more positive test reactions. Seven of these patients (20%) had one or more clinically relevant positive reactions, most often to flavours and

spices. **CONCLUSION:** A considerable number of patients with anogenital dermatitis have a contact sensitization. Clinically relevant reactions were mainly found to spices and flavours. This is in contrast to the data reported in the literature that shows most contact allergies in vulval patients to ingredients of topical medication.

## **Basic Science**

### **The course and branching pattern of pudendal nerve in fetus.**

Kocabiyik N, Tatar I, Yalcin B, Ozan H  
Clin Anat. 2008 Oct;21(7):691-5

The pudendal nerve is a considerably large branch of the sacral plexus. There are many articles in the literature concerning the pudendal nerve in adults, but as far as we know, there is none on the branching pattern and variations in pudendal nerve anatomy in fetus. This study investigates the pudendal nerve trunking with respect to the piriformis muscle in 25 formalin-fixed fetuses (50 sides of pelves, 15 females, 10 males), ranging from 20 to 37 weeks of gestation. We investigate pudendal nerve trunking in four types: Type I-a is defined as single-trunk with the inferior rectal nerve branching proximal to the dorsal nerve of penis/clitoris (38%), Type I-b is also single-trunk with the dorsal nerve of penis/clitoris branching proximal to the inferior rectal nerve (24%), Type II is double-trunk with medial trunk as an inferior rectal nerve (34%), and Type III is triple-trunk (4%). We measured the average diameter of the main trunk of pudendal nerve in Type I-a and I-b groups to be 0.98 +/- 0.33 mm. We also measured the average length of the pudendal nerve trunks before the dorsal nerve of penis/clitoris branch to be 7.35 +/- 3.50 mm. There was no significant statistical difference in the average length, diameter, number of trunks, and pudendal nerve variations between male and female and also right and left sides of the pelves. This first and detailed fetal study of pudendal nerve trunking with respect to the piriformis muscle would be useful for educational anatomy dissections and anatomical landmark definitions for relevant clinical procedures.

### **The contribution of the levator ani nerve and the pudendal nerve to the innervation of the levator ani muscles; a study in human fetuses.**

Wallner C, van Wissen J, Maas CP, Dabhoiwala NF, DeRuiter MC, Lamers WH  
Eur Urol. 2008 Nov;54(5):1136-42

**OBJECTIVES:** The contributions of the pudendal and levator ani nerves to the innervation of the levator ani muscle (LAM) are disputed. Because of the relatively large size of the nerves in early life, we investigated this issue in human fetuses. **METHODS:** (Immuno)histochemically stained serial sections of nine human fetuses (9-22 wk of gestation) were investigated. Both the left and right sides of the fetal pelves were studied individually and 3D reconstructions were prepared. **RESULTS:** The levator ani nerve innervated the LAM in every pelvis, whereas a contribution of the pudendal nerve to the innervation of the LAM could be demonstrated in only 10 pelvic halves (56%). In 10 halves, we observed a communicating nerve branch between the pudendal and levator ani nerves that pierced the pelvic floor between the LAM and the coccygeus muscle. No sex differences were observed, but the innervation pattern did differ between the left and right side of a pelvis. **CONCLUSIONS:** The LAM often has a dual somatic innervation with the levator ani nerve as its constant and main neuronal supply.

### **Structure, innervation, mechanical properties and reflex activation of a striated sphincter in the vestibule of the cat vagina.**

Lagunes-Cordoba R, Tsutsumi V, Munoz-Martinez E  
Reproduction. 2008 Dec 2. [Epub ahead of print]

Vaginal constriction might be important for reproduction in mammals, but existing information is both limited and controversial. This paper shows the structure, mechanical properties, innervation and reflex

response of a striated sphincter in the vestibule of the cat vagina. A Foley catheter coupled to pressure transducer detected in the lumen of the vestibule a pressure wave that was induced by stimulation of the external branch of the motor pudendal nerve. The peak pressure of the wave induced by bilateral stimulation (30.6 cm H<sub>2</sub>O) was about double of the peak pressure wave induced unilaterally. The tetanus/twitch amplitude ratio was 4.5. The sphincter that produces the increase in vaginal pressure fatigues slowly. Digital, point-to-point summation of unilateral waves was greater than the wave induced bilaterally. Summation of the pressure wave induced by the separate stimulation of the terminal motor branches was also greater than the wave induced by the entire motor nerve. This might reflect multiple innervation of muscle fibres. Single, controlled probing of the vaginal vestibule induced a reflex discharge in the motor nerve. Repetitive probing (10 Hz) induced a motor nerve post-discharge lasting > 1 min. The vaginal sphincter is two-half rings of striated muscle fibres in the wall of the vaginal vestibule; the fibres end freely in the dorsal and ventral midlines. Penetration of the vestibule by the penis might trigger sustained contraction of the vaginal sphincter.

### **Ultrasonographic and doppler velocimetric evaluation of the levator ani muscle according to the hormonal status.**

Noguti AS, Jarmy-Di Bella ZIK, de Oliveira E, Castro RA, Lima GR, Baracat EC, Sartori MGF, Girão MJBC

Eur J Obstet Gynecol Reprod Biol. 2008 Dec;141(2):183-5.

**OBJECTIVE:** We aimed to study the cross-sectional area of levator ani muscle and the doppler velocimetric parameters of vessels its in premenopausal and postmenopausal women. **STUDY DESIGN:** Sixty-four patients, divided into 3 groups, were assessed: group I (20 women-average age 28 years) premenopausal and nulliparous (control); group II (24 women-average age 38 years, vaginal delivery 1-4) premenopausal with vaginal deliveries; group III (20 women-average age 55 years, parity 0-4) postmenopausal without hormonal therapy. Doppler velocimetry of levator ani muscle vessels through resistance and pulsatility indices was used and the means of the groups compared by adjusting the weighed variance model with multiple comparisons, according to Tukey's method. Similarly, we measured the cross-sectional area of the muscle using ultrasonography. **RESULTS:** There was a significant increase in resistance and pulsatility indices in postmenopausal patients as compared to the other two groups. We also observed a significant decrease in the cross-sectional area of the muscle of postmenopausal patients when compared to those in premenopausal. **CONCLUSION:** The obtained results allow us to conclude that levator ani muscle vascularization significantly decreases after menopause (age and/or hipoestrogenism) and that it can be assumed that vaginal delivery does not promote long-term alterations in levator ani muscle vascularization. We also observed a significant decrease in the cross-sectional area of the muscle in postmenopausal women when compared to those in premenopausal.