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This newsletter is quarterly and contains abstracts from medical journals published between January and March 2008 (abstracts presented at scientific meetings may also be included). Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia

Association between primary vulvar vestibulitis syndrome, defective induction of tumor necrosis factor-alpha, and carriage of the mannose-binding lectin codon 54 gene polymorphism.
Babula O, Linhares IM, Bongiovanni AM, Ledger WJ, Witkin SS
Am J Obset Gynecol. 2008 Jan;198(1):101.e1-101.e4

OBJECTIVE: We evaluated whether women with vulvar vestibulitis syndrome (VVS) could be subdivided on the basis of genotyping the polymorphic mannose-binding lectin (MBL) gene. STUDY DESIGN: DNA from 123 women with VVS was tested for a single nucleotide polymorphism at codon 54 of the MBL gene. Blood samples from 86 of the women were evaluated for ex vivo tumor necrosis factor-alpha (TNF-alpha) and interleukin-1 receptor antagonist (IL-1ra) production in response to Candida albicans, Gram-positive peptidoglycan, and Gram-negative lipopolysaccharide. Associations between laboratory findings and clinical characteristics were analyzed. RESULTS: The variant MBL*B allele was identified in 33 subjects (26.8%). This polymorphism was more prevalent in women whose symptoms developed at their first act of sexual intercourse (primary VVS, 40.9%), as opposed to women with secondary VVS (16.3%; P = .01). Ex vivo TNF-alpha production, but not IL-1ra production, was reduced in MBL*B carriers as compared with MBL*A homozygotes (P </= .03). CONCLUSION: The MBL gene polymorphism is associated with the development of primary VVS and a reduced capacity for TNF-alpha production in response to microbial components.

Involvement of heparanase in the pathogenesis of localized vulvodynia.
Bornstein J, Cohen Y, Zarfati D, Sela S, Ophir E
Int J Gynecol Pathol. 2008 Jan;27(1):136-41

SUMMARY: Recently, we have shown that vestibular hyperinnervation and the presence of 8 or more mast cells in a 10 x 10 microscopic field can be used as diagnostic criteria in localized vulvodynia (vulvar vestibulitis). We have also documented that degranulation of mast cells occurs in these cases. The present study further examines the characteristics of vestibular hyperinnervation and mast cell function in localized vulvodynia to elucidate if the 2 processes-hyperinnervation and mast cell increase and degranulation-are related. We examined vestibular tissue from 7 women aged 18 to 48 with severe localized vulvodynia and from 7 healthy control women. Parallel sections were stained by Giemsa and then immunostained for CD117 and heparanase. Nerve fibers that expressed protein gene product 9.5 were examined. Tissues from women with localized vulvodynia documented a significant increase in vestibular mast cells, subepithelial heparanase activity, and intraepithelial hyperinnervation compared with healthy women. This is the first documentation of heparanase activity in localized vulvodynia. Heparanase, which is degranulated from mast cells, is capable of degrading the vestibular stroma and epithelial basement membrane, thus permitting stromal proliferation and intraepithelial extension of nerve

fibers, as seen in the present study. The hyperinnervation has been thought to cause the vestibular hyperesthesia distinctive of localized vulvodynia.

Steroid receptor expression and morphology in provoked vestibulodynia.
Johannesson U, Sahlin L, Masironi B, Hilliges M, Blomgren B, Rylander E, Bohm-Starke N
Am J Obstet Gynecol. 2008 Jan 4 [Epub ahead of print]

OBJECTIVE: This study was undertaken to survey the steroid receptor expression and morphology in the vulvar vestibular mucosa in women with provoked vestibulodynia. STUDY DESIGN: Fourteen patients and 25 controls without oral contraceptives were included. Vestibular biopsy specimens were obtained and analyzed by using immunohistochemistry, followed by computerized image analysis of estrogen receptors alpha and beta, progesterone receptors A and B, glucocorticoid receptor, androgen receptor, and the proliferation marker Ki67. The morphology was estimated by measuring 4 parameters in the epithelium. RESULTS: There was a significantly higher expression of estrogen receptor alpha in both the epithelium (P = .04) and the stroma (P = .02) in the patient specimens compared with the controls. There were no significant differences in the other analyses performed. CONCLUSION: There is an increased expression of estrogen receptor alpha in the vestibular mucosa but the epithelial morphology seems unaffected in women with provoked vestibulodynia. Further studies regarding plausible associations to neurogenic inflammation are needed.

Influence of oral contraceptive use on the risk of adult-onset vulvodynia.
Harlow BL, Vitonis AF, Stewart EG
J Reprod Med 2008;53:102-110

OBJECTIVE: To examine the association of adult-onset vulvodynia with oral contraceptive use. STUDY DESIGN: We conducted a population-based study of 177 women experiencing vulvar pain consistent with clinical criteria for vulvodynia and community-matched controls. Analyses were repeated and validated in clinically confirmed clinic- based and population-based cases and matched controls. RESULTS: In our analyses of population-based cases and controls, oral contraceptive use was associated with a nonsignificant, 30% increase in the risk of vulvodynia (95% CI 0.7–2.3) and was highest among women whose first use occurred before age 18 (OR=2.5, 95% CI 1.1–5.8). These findings were similar when restricted to clinically confirmed cases. CONCLUSION: These findings do not support the strong associations observed in clinic-based studies. In our study, clinically confirmed clinic-based cases, as compared to population-based cases, were more often oral contraceptive users, earlier-age users and users for longer periods. Thus, observational studies using clinic-based cases might not adequately represent oral contraceptive use in all women with vulvodynia.

The treatment of provoked vestibulodynia: a critical review.
Landry T, Bergeron S, Dupuis MJ, Desrochers G
Clin J Pain. 2008 Feb;24(2):155-71

OBJECTIVE: To carry out a critical review of published studies concerning the treatment of provoked vestibulodynia. METHODS: MEDLINE, PsycINFO, and Cochrane were used to identify treatment studies published between January 1996 and December 2006. All studies published in English that dealt specifically with the treatment of provoked vestibulodynia were included in the review regardless of their methodological quality. Thirty-eight treatment studies were thus examined in the present paper. RESULTS: Since 1996, surgical treatment has received somewhat less empirical attention. Nevertheless, it still boasts the best success rates, which range from 61% to 94%. More studies have focused on medical treatments, yielding success rates varying between 13% and 67%. Behavioral treatments have been the least studied, although 35% to 83% of patients benefit from them. Despite these interesting results, only 5 of the 38 treatment studies reviewed are randomized clinical trials. Furthermore, the majority of studies have several methodological weaknesses, such as the absence of (1) control or placebo group, (2) double-blind evaluation, (3) pretreatment pain evaluation, and (4) validated measures

of pain and sexual functioning. DISCUSSION: On the basis of the results of the reviewed prospective studies and the randomized clinical trials, vestibulectomy is the most efficacious treatment to date. Though some medical treatments seem little effective, others appear promising and should be investigated further, as is the case with behavioral treatments. Additional randomized clinical trials are necessary to confirm the efficacy of surgery and validate nonsurgical treatments for provoked vestibulodynia.

Surgery for localized, provoked vestibulodynia: a long-term follow-up study.
Bohm-Starke N, Rylander E
J Reprod Med 2008; 53:83–89

OBJECTIVE: To evaluate the long-term results of vestibulectomy in women with localized, provoked vestibulodynia. STUDY DESIGN: A retrospective questionnaire survey was filled out by 67 Swedish women who underwent surgery for localized, provoked vestibulodynia during 1992–2003. The questionnaire was completed a minimum of 12 months after the operation. Coital pain, quality of sexual life and psychologic well-being were evaluated. RESULTS: The mean age at the time of surgery was 27 years (18–56) and the median follow-up time 41 months (12–120). Coital pain, rated with Visual Analogue Scales (VASneg) (0–10), was 8.0 (median) before surgery, 5.0 ($p<0.001$) 6 months after surgery and 2.0 ($p<0.001$) at follow-up. Quality of sexual life, using VASpos (10–0), was 6.5 (median) before dyspareunia, 0.5 ($p<0.001$) prior to surgery and 6.5 ($p<0.001$) at follow-up. Complete or major improvement was reported by 56% of women with secondary vestibulodynia and 17% of women with primary vestibulodynia ($p=0.03$). Improved psychologic well-being was reported by 79%. CONCLUSION: Women with secondary localized provoked vestibulodynia will often benefit from surgery when other treatments fail. Surgical outcome should include both pain relief and psychosexual well-being. In this study women with primary vestibulodynia were less likely to benefit from surgery.

Surgical and behavioral treatments for vestibulodynia: two-and-one-half year follow-up and predictors of outcome.
Bergeron S, Khalife S, Glazer HI, Binik YM
Obstet Gynecol. 2008 Jan;111(1):159-166

OBJECTIVE: To estimate whether treatment gains for provoked vestibulodynia participants randomly assigned to vestibulectomy, biofeedback, and cognitive-behavioral therapy in a previous study would be maintained from the last assessment-a 6-month follow-up-to the present 2.5-year follow-up. Although all three treatments yielded significant improvements at 6-month follow-up, vestibulectomy resulted in approximately twice the pain reduction as compared with the two other treatments. A second goal of the present study was to identify predictors of outcome. METHODS: In a university hospital, 51 of the 78 women from the original study were reassessed 2.5 years after the end of their treatment. They completed 1) a gynecologic examination involving the cotton-swab test, 2) a structured interview, and 3) validated pain and sexual functioning measures. RESULTS: Results from the multivariate analysis of variance conducted on the pain measures showed a significant time main effect ($P<.05$) and a significant treatment main effect ($P<.01$), indicating that participants had less pain at the 2.5-year follow-up than at the previous 6-month follow-up. Results from the multivariate analysis of variance conducted on sexual functioning measures showed that participants remained unchanged between the 6-month and 2.5-year follow-up and that there were no group differences. Higher pretreatment pain intensity predicted poorer outcomes at the 2.5-year follow-up for vestibulectomy ($P<.01$), biofeedback ($P<.05$), and cognitive-behavioral therapy ($P<.01$). Erotophobia also predicted a poorer outcome for vestibulectomy ($P<.001$). CONCLUSION: Treatment gains were maintained at the 2.5-year follow-up. Outcome was predicted by pretreatment pain and psychosexual factors. LEVEL OF EVIDENCE: II.

Bladder and bowel symptoms among women with vulvar disease: are they universal?
Kennedy CM, Nygaard IE, Bradley CS, Galask RP
J Reprod Med 2007;52:1073–1078

OBJECTIVE: To compare the prevalence of painful bladder syndrome, recurrent urinary tract infections, urinary leakage and irritable bowel syndrome between women with specific vulvar disorders and controls. STUDY DESIGN: Women with a primary diagnosis of vulvar intraepithelial neoplasia (dysplasia), vulvar vestibulitis (vestibulitis), contact vulvitis, atrophic vulvovaginitis, lichen simplex, lichen sclerosus and lichen planus, were compared to women presenting for annual examinations. RESULTS: As compared to controls, painful bladder syndrome was more prevalent among subjects with dysplasia, vestibulitis and contact vulvitis; a history of recurrent urinary tract infection was more prevalent among subjects with contact vulvitis; and urinary incontinence was less prevalent in subjects with lichen sclerosus. Irritable bowel syndrome was more prevalent among subjects with dysplasia, vestibulitis, lichen sclerosus, lichen planus and lichen simplex than controls. CONCLUSION: The prevalence of bladder and irritable bowel symptoms varies between vulvar disorders.

Overlap between orofacial pain and vulvar vestibulitis syndrome.
Zolnoun DA, Rohl J, Moore CG, Perinetti-Liebert C, Lamvu GM, Maixner W
Clin J Pain. 2008 March/April;24(3):187-191

OBJECTIVES: To explore the prevalence of orofacial pain (OFP) among patients with vulvar vestibulitis syndrome (VVS) and to examine the relationship between signs and symptoms of OFP and clinical characteristics of women with VVS, we investigated differences in psychologic characteristics and severity of painful intercourse. METHODS: In this cross-sectional exploratory study, 137 women with VVS completed questionnaires that assessed levels of pain, anxiety, somatization, and presence of signs and symptoms suggestive of clinical and subclinical OFP. Demographic data were gathered from medical records. RESULTS: OFP was found to be a highly prevalent (78%) condition among women with VVS. Compared with women who had no OFP symptoms (n=30), those with symptoms (n=64) reported higher levels of anxiety (45.0 vs. 37.8, Bonferroni adjusted P=0.017), somatization (125.2 vs. 96.0, Bonferroni adjusted P<0.001), and psychologic distress (62.8 vs. 56.0, Bonferroni adjusted P=0.002). Although we observed a similar trend among women with subclinical OFP (n=43), this trend only reached statistical significance with respect to somatization. Differences were not detected for demographics, duration of pain, and severity of pain during intercourse across the 3 groups. DISCUSSION: OFP is a common condition among women with VVS. Because severity and duration of painful intercourse did not differ by OFP classification but psychologic characteristics did, we must begin to question a unidimensional focus on vestibular mucosa as a reason for pain and persistent distress.

Insight into urogynecologic features of women with interstitial cystitis/painful bladder syndrome.
Gardella B, Porru D, Ferdeghini F, Martinotti Gabellotti E, Nappi RE, Rovereto B, Spinillo A
Eur Urol. 2008 Feb 6 [Epub ahead of print]

OBJECTIVE: The prevalence of interstitial cystitis/painful bladder syndrome (IC/PBS) among gynecologic patients attending vulvar disease or pelvic pain clinics is higher than expected. The evaluation of gynecologic characteristics in patients with IC/PBS could be important to delineate a better therapeutic strategy. METHODS: We compared clinical gynecologic characteristics including localized and generalized vulvodynia and sexual activity of 47 women with a definite diagnosis of IC/PBS versus 47 negative controls. RESULTS: The prevalence of both generalized or localized vulvodynia was 85.1% (40 of 47) in the patients and 6.4% (3 of 47) in the control group (p<0.0001 by Fisher exact test). The mean visual analogue score on generalized or localized vulvodynia evaluated with the cotton swab test was 6.1+/-2.6 (SD) among women with IC/PBS and 0.6+/-1.7 in the control group (p<0.0001 with Mann-Whitney U test). Pain during intercourse was described as unbearable by 15 women with IC/PBS (31.9%) and 2 controls (4.3%; p=0.001 by Fisher exact test). Sexual function was significantly impaired in women with IC as measured by the median total score of the Female Sexual Function Index in comparison with controls (13.8 vs. 28.7; p<0.0001). CONCLUSIONS: Patients with a definite diagnosis of IC/PBS appear to have a high risk of vulvodynia with the associated negative implications for sexual activity. The establishment of a multidisciplinary approach with the involvement of the gynecologist appears to be a logical requisite for a correct treatment strategy for these patients.

Spinal cord stimulator for the treatment of a woman with vulvovaginal burning and deep pelvic pain.
Nair AR, Klapper A, Kushnerik V, Margulis I, Del Priore G
Obstet Gynecol. 2008;111:545-7.

BACKGROUND: Vulvodynia is a chronic pain disorder of the vulva that occurs in the absence of visible infectious, inflammatory, neoplastic, or neurological findings. Multiple treatment modalities are used, often with insufficient results. We report the successful use of a spinal cord stimulator to treat vulvodynia symptoms in a patient who had unsuccessful prior conservative therapies. CASE: A postmenopausal woman presented with 15 years of treatment for vulvar and vaginal burning and deep pelvic pain. She had been taking multiple pain medications with inadequate relief. After successful test stimulation, a permanent spinal cord stimulator was implanted. At 10 months posttreatment, her pain improved by 80%, and the patient no longer requires oral medication.
CONCLUSION: The use of spinal cord stimulation was successful in a patient with vulvodynia and unsuccessful multiple prior therapies and whose symptoms were diffuse in nature.

Vulvodynia (CME).
Goldstein AT, Burrows L
J Sex Med. 2008 Jan;5(1):5-15

Introduction. Vulvodynia is increasingly recognized as a cause of sexual pain. Aim. The goal of this Continuing Medical Education article was to provide a comprehensive review of vulvodynia including terminology, possible etiologies, and offer treatment options. Methods. A Medline search was conducted using several terms related to and including the terms vulvodynia, vulvar vestibulitis, vestibulodynia, and pudendal neuralgia. Results. A thorough review of vulvodynia. Conclusion. Vulvodynia most likely represents several disorders without an identifiable cause in many cases. The management of these patients requires a sensitive provider who can coordinate a multidisciplinary approach to their care. Despite the lack of large-scale, placebo-controlled trials, several new treatment options exist.

Vulvodynia.
Hoffstetter S, Leong FC, LeFebre C
Mo Med. 2007 Nov-Dec;104(6):522-5

Vulvar pain and discomfort are common conditions which can truly make the patient's life miserable. It is relatively common, but can be a difficult condition to evaluate and treat. This article serves to give the primary care physician a basic framework with which to begin treatment for such patients.

Vulvodynia: a psychophysiological profile based on electromyographic assessment.
Jantos M
Appl Psychophysiol Biofeedback. 2008 Jan 24 [Epub ahead of print]

The objective of this study was to explore the relationship between psychological and physiological processes and how these interact in the case of vulvodynia. The study design consisted of a retrospective review of predominantly premenopausal women presenting with vulvodynia via analyses of questionnaires, psychometric tests, sexual history, surface electromyographic (sEMG) assessments, and clinical notes. Five hundred and twenty-nine patients with vulvodynia (mean age 27.7 years) were studied. The average age of symptom onset was 22.8 years and the average duration of symptoms was 5.0 years. Patients scored higher than the comparison group on global dimensions of the Symptom Checklist-90 Revised (SCL-90R), with anxiety and depression scores showing a significant but modest correlation with severity of pain. sEMG data confirmed an association with pelvic muscle dysfunction but there was no correlation with severity of vulvar pain. A negative correlation between sEMG readings and duration of pain was noted and may be due to progressive time-related quieting of electrical activity in muscle tissues, which is commonly associated with the development of a functional muscle contracture.

In conclusion, it is important to view chronic pain syndromes like vulvodynia from a psychophysiological perspective which recognizes the potential contribution of psychological and physiological variables in the aetiology of chronic vulvar pain.

Psychosocial impact of chronic vulvovaginal conditions.
Jelovsek JE, Walters MD, Barber MD
J Reprod Med 2008;53:75-82

OBJECTIVE: To describe the degree of psychosocial impairment resulting from chronic vulvovaginal disorders (VVDs). STUDY DESIGN: Seventy-five consecutive women suffering from a chronic VVD were recruited and classified using current International Society for the Study of Vulvovaginal Disease (ISSVD) classification criteria. They completed a 69-item, self-administered, comprehensive questionnaire to assess the impact of chronic VVD on psychosocial functioning and quality of life. Summary scores were calculated for 5 domains including pain, body image, relationships, emotion, quality of life and sexual function. RESULTS: After adjusting for age and duration of vulvovaginal symptoms, women with vulvodynia were more likely than women with other chronic VVDs to score significantly worse on relationship ($p<0.001$), emotion ($p<0.03$) and physical activity ($p=0.001$) areas. The majority of subjects suffered from a worsening impact of sexual function, and no differences were detected between the groups. The overall intensity of vulvar or vaginal pain correlated weakly with the degree of psychosocial impairment in the domains of relationships, emotion and physical quality of life. CONCLUSION: Differences in quality of life exist between women with vulvodynia and those with other chronic VVDs. The presence, not the intensity, of vulvovaginal pain correlates with degree of psychosocial impairment.

Psychosexual characteristics of vestibulodynia couples: partner solicitousness and hostility are associated with pain.
Desrosiers M, Bergeron S, Meana M, Leclerc B, Binik YM, Khalife S
J Sex Med. 2007 Dec 17 [Epub ahead of print]

Introduction. Provoked vestibulodynia is a prevalent yet misunderstood women's sexual health issue. In particular, data concerning relationship characteristics and psychosexual functioning of partners of these women are scarce. Moreover, no research to date has examined the role of the partner in vestibulodynia. Aims. This study aimed to characterize and compare the psychosexual profiles of women with vestibulodynia and their partners, in addition to exploring whether partner-related variables correlated with women's pain and associated psychosexual functioning. Methods. Forty-three couples in which the woman suffered from vestibulodynia completed self-report questionnaires focusing on their sexual functioning, dyadic adjustment, and psychological adjustment. Women were diagnosed using the cotton-swab test during a standardized gynecological examination. They also took part in a structured interview during which they were asked about their pain during intercourse and frequency of intercourse. They also completed a questionnaire about their perceptions of their partners' responses to the pain. Main Outcome Measures. Dependent measures for both members of the couple included the Sexual History Form, the Locke-Wallace Marital Adjustment Scale and the Brief Symptom Inventory. Women completed a horizontal analog scale assessing the intensity of their pain during intercourse and reported their frequency of intercourse per month. Results. Findings show that women with vestibulodynia and their partners did not differ from population norms with regard to global sexual functioning, dyadic adjustment and psychological adjustment. However, mean frequency of intercourse was lower than the standard for this age group. Also, women had significantly poorer sexual functioning than men. In addition, a regression analysis revealed that partner solicitousness and hostility were significantly associated with higher levels of pain during intercourse. Conclusions. Results suggest that although the psychosexual and relationship characteristics of partners of women with vestibulodynia are within norms, their responses may play a role in the experience of pain.

Life events in patients with vulvodynia.
Plante AF, Kamm MA
BJOG.2008 Mar;115(4):509-14

OBJECTIVE: Vulval pain, in the absence of pathology, may have a psychological basis that relates to life events. This study aimed to determine the nature of such events. DESIGN: Structured questionnaire about patient's symptoms and early-life events. SETTING: Private practice physiotherapist specialising in pelvic floor disorders. POPULATION: Patients with vulvodynia as their primary symptom and control patients being treated for urinary tract disorder or post-childbirth routine physiotherapy who had no vulval pain on direct questioning. METHODS: Questionnaire applied to consecutive patients referred for treatment. Seventy-eight consecutive women presenting with vulvodynia (mean age 34 years, mean duration of symptoms 48 months) and 78 controls (mean age 39 years). MAIN OUTCOME MEASURES: Incidence of life events. RESULTS: A similar proportion of both groups were married. Being in a new relationship (P < 0.04), adverse current or previous relationships (39 versus 9%, P < or = 0.01), parental divorce (26 versus 9%, P < or = 0.001), history of termination of pregnancy, and adverse childbirth experiences (P < 0.04) were more common in patients than in controls. A history of sexual abuse was not more common in patients with vulvodynia compared with controls (13 versus 10%, P = not significant). Lack of libido was common in patients with vulvodynia (94 versus 29%, P < 0.0001). CONCLUSIONS: Adverse life experiences, including conflict, are common in women with vulvodynia. These factors may be important in mediating the genesis of pain through stress-related mechanisms. Sexual interest is diminished in these women. Sexual abuse is not a factor in most of these women. These findings have implications for treatment.

Other Vulvovaginal Disorders

Early onset vulvar lichen sclerosus in premenopausal women and oral contraceptives.
Gunthert AR, Faber M, Knappe G, Hellriegel S, Emons G
Eur J Obstet Gynecol Reprod Biol. 2008 Mar;137(1):56-60. Epub 2007 Dec 4.

OBJECTIVE: For vulvar Lichen sclerosus (LS) immunological factors, genetic predisposition, and decreased 5 alpha-reductase activity have been discussed as aetiological factors. During the last decade an increase of LS in young women has been suspected. Aim of this study was to evaluate data of premenopausal women with early onset LS to find potential risk factors focussing on the use of oral contraceptives. STUDY DESIGN: We retrospectively analyzed the data of 40 premenopausal patients with early onset LS regarding use of oral contraceptives (OCPs), and first occurrence of LS. To compare these data in a case-control study we analyzed a matched control group of 110 healthy women. RESULTS: All our LS patients were using OCPs compared to 73 women (66.4%) in the control group. OCPs with anti-androgenic activity (chlormadinone acetate, cyproterone acetate, dienogest, and drospirenone) were used by 28 (70%) of the LS patients and by 35 (47.9%) of the 73 women using OCPs in the control group. Thus, the odds ratio for early onset LS for women using anti-androgenic OCPs was 2.53 (95% CI: 1.12-5.75). CONCLUSION: Our data suggest that disturbance of the androgen dependent growth of the vulvar skin by OCPs and especially by OCPs with anti-androgenic properties might trigger the early onset of LS in a subgroup of susceptible young women.

Vulvar lichen sclerosus: effect of maintenance treatment with a moisturizer on the course of the disease.
Simonart T, Lahaye M, Simonart JM
Menopause. 2008 Jan-Feb;15(1):74-7.

OBJECTIVES: Vulvar lichen sclerosus (LS) is an inflammatory disease of unknown etiology that may result in significant discomfort and psychological distress in postmenopausal women. One of the most troublesome features of LS is its chronically relapsing nature. The aim of this study was to investigate the effect of maintenance therapy with a moisturizer in preventing the risk of relapse and progression of

vulvar LS in postmenopausal women. DESIGN: Between January 1995 and January 2006, 34 postmenopausal women with vulvar LS were included in a prospective open trial. The participants were treated with a topical corticosteroid cream (0.1% betamethasone valerate) once daily for 1 month and then with maintenance therapy with a moisturizing cream alone once daily. Follow-up visits were scheduled after 1 month and then twice per year (median follow-up, 58 mo). RESULTS: Overall the symptoms of all women improved after therapy with a topical steroid. Twenty-four women (71%) became symptom free, and 10 (29%) experienced partial response. Eighteen of the 24 women (75%) who became symptom free and 6 of the 10 women (60%) who exhibited a partial response reported no worsening of their symptoms while on therapy with a cold cream alone. Total resolution of the clinical signs occurred in 6 of the 19 women with mild vulvar architectural changes. Partial resolution of clinical signs was observed in 22 women (64%). No change was noticed in six (18%) women. None of the participants experienced worsening of vulvar scarring. None of the participants developed vulvar intraepithelial neoplasia or squamous cell carcinoma during the follow-up period. There were no side effects. CONCLUSION: Long-term maintenance therapy of vulvar LS with a moisturizing cream can maintain the symptom relief induced by topical corticosteroids in women with vulvar LS while being safe and inexpensive. This treatment may also be associated with a reduction in topical corticosteroid use because more than half of the women could eliminate corticosteroids altogether.

Efficacy of low-dose estradiol vaginal tablets in the treatment of atrophic vaginitis: a randomized controlled trial.
Bachmann G, Lobo RA, Gut R, Nachtigall L, Notelovitz M
Obstet Gynecol. 2008 Jan;111(1):67-76

OBJECTIVE: To evaluate the efficacy of two vaginal doses of estradiol (E2) compared with placebo in the treatment of atrophic vaginitis. METHODS: In a multi-center, randomized, double-blind, parallel-group study, 230 postmenopausal women received treatment with 25 mcg or 10 mcg E2 or placebo for 12 weeks. Efficacy was measured through composite score of three vaginal symptoms and grading of vaginal health. Additional analyses included maturation of vaginal and urethral mucosa. Safety assessments included endometrial biopsy, adverse events, changes in laboratory tests, and physical examinations. After 12 weeks of treatment, all patients were switched to the open-label extension and received treatment with 25 mcg E2 up to week 52. RESULTS: Vaginal tablets with 25 mcg and 10 mcg E2 showed significant (P<.001) improvement in composite score of vaginal health. Other results with 10 mcg E2 were not entirely consistent with those for 25 mcg E2. Over 12 weeks, both active treatments resulted in greater decreases in vaginal pH than placebo. There were no significant differences between the 25 mcg and 10 mcg E2 groups in terms of improvements in maturation value or composite score of three vaginal symptoms. The efficacy was maintained to week 52 with 25 mcg E2. CONCLUSION: Vaginal tablets with 25 mcg and 10 mcg E2 provided relief of vaginal symptoms, improved urogenital atrophy, decreased vaginal pH, and increased maturation of the vaginal and urethral epithelium. Those improvements were greater with 25 mcg than with 10 mcg E2. Both doses were effective in the treatment of atrophic vaginitis. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, www.clinicaltrials.gov, NCT00465192 and NCT00464971 LEVEL OF EVIDENCE: I.

Desquamative inflammatory vaginitis: what is it?
Murphy R, Edwards L
J Reprod Med 2008;53:124–128

OBJECTIVE: To record the inflammatory patterns found in desquamative inflammatory vaginitis and to investigate further the existence of an idiopathic subset of this condition. STUDY DESIGN: This was a retrospective case note study of 11 women over a 12-month period who presented with symptoms of painful sexual intercourse and increased vaginal discharge. RESULTS: Examination of the vulva was usually normal or showed mild erythema and a thin purulent discharge. Examination of the vaginal wall showed erythema consistent with inflammation. A biopsy from the vag- inal wall showed essentially 2 patterns of inflammation: either a lichenoid or a nonspecific mixed inflammatory infiltrate. Therapy with clindamycin and clobetasone propionate was largely effective. CONCLUSION: While this study does not

fully answer the histology of desquamative inflammatory vaginitis, it does highlight the need for further study to identify whether there is an idiopathic subset of desquamative inflammatory vaginitis or whether it is erosive lichen planus.

The vulvar dermatoses.
Burrows LJ, Shaw HA, Goldstein AT
J Sex Med.2008 Feb;5(2):276-83. Epub 2008 Jan 2

Introduction. Dermatologic diseases of the vulva may cause dyspareunia. These disorders may be overlooked by gynecologists and urologists because of lack of residency training experience. Dermatologists who are most familiar with these diseases are infrequently trained in vulvovaginal examination. As such, these disorders are often improperly diagnosed and treated. Aim. To describe the presentation and management of the major vulvar dermatoses including irritant and allergic contact dermatitis, lichen sclerosus, lichen simplex chronicus, and lichen planus. Main Outcome Measure. Data from a peer review literature search on the topic of vulvar dermatoses. Methods. The literature for this review article was obtained through a Medline search. Appropriate dermatology textbooks were utilized for additional information. Results. A comprehensive survey of the vulvar dermatoses. Conclusion. Vulvar dermatoses must be considered a part of the differential diagnosis of any woman with a sexual pain disorder. As such, healthcare providers who evaluate and treat women with dyspareunia must become familiar with the most common dermatologic disorders of the vulva.

Non-neoplastic epithelial disorders of the vulva.
O'Connell TX, Nathan LS, Satmary WA, Goldstein AT
Am Fam Physician. 2008 Feb 1;77(3):321-6

Lichen sclerosus, lichen planus, and lichen simplex chronicus are three of the most common non-neoplastic epithelial disorders of the vulva. Lichen sclerosus is characterized by intense vulvar itching and can affect men and women of all ages, but it manifests most commonly in postmenopausal women. Patients with lichen sclerosus have an increased risk of developing squamous cell carcinoma, and they should be monitored for malignancy. Lichen planus is an inflammatory autoimmune disorder that can affect the vulva and the vagina; it peaks in incidence between ages 30 and 60. There are three clinical variants of lichen planus affecting the vulva: erosive, papulosquamous, and hypertrophic. Lichen simplex chronicus is caused by persistent itching and scratching of the vulvar skin, which results in a thickened, leathery appearance. It is thought to be an atopic disorder in many cases and may arise in normal skin as a result of psychological stress or environmental factors. Definitive diagnosis of non-neoplastic disorders depends on the histology of biopsied tissue. All three disorders are treated with topical corticosteroid ointments of varying potency. Lichen sclerosus and lichen planus are not routinely treated with surgery, which is necessary only in patients who have a malignancy or advanced scarring that causes dyspareunia or clitoral phimosis. Educational counseling teaches patients that even though these chronic disorders cannot be cured, they can be effectively managed.

Itraconazole vs fluconazole for the treatment of uncomplicated acute vaginal and vulvovaginal candidiasis in nonpregnant women: a metaanalysis of randomized controlled trials.
Pitsouni E, Iavazzo C, Falagas ME
Am J Obstet Gynecol. 2008 Feb;198(2):153-60

In this metaanalysis of randomized controlled trials (RCTs) we aimed to compare the in vivo and in vitro activity and the safety of per os itraconazole and fluconazole treatment of uncomplicated acute vaginal/vulvovaginal candidiasis in nonpregnant women. We used PubMed, Scopus, Web of Science, and Cochrane Library to identify the studies that were relevant to our metaanalysis RCTs. Six RCTs were included in this study that comprised 1092 enrolled patients with signs and symptoms of vaginal/vulvovaginal candidiasis that was confirmed by microscopy and/or microbiologic cultures that were obtained from the ectocervix and/or vaginal fundus. Overall, there was no difference between

itraconazole and fluconazole regarding clinical cure and improvement at the first and second scheduled visit assessments (pooled odds ratio [OR], 0.94 [95% CI, 0.6-1.48] and 1.09 [95% CI, 0.68-1.75], respectively), mycologic cure at the first and second scheduled visit assessments (OR, 0.73 [95% CI, 0.31-1.7] and 0.71 [95% CI, 0.49-1.03], respectively), withdrawal of patients because of severe adverse events (OR, 0.72 [95% CI, 0.16-3.32]), and adverse events noted from the nervous and digestive systems (OR, 1.07 [95% CI, 0.42-2.73] and 1.84 [95% CI, 0.3-11.27], respectively). In conclusion, effectiveness and safety of oral itraconazole and fluconazole in the treatment of acute uncomplicated vaginal/vulvovaginal candidiasis are similar.

MBL2 genetic screening in patients with recurrent vaginal infections.
Milanese M, Segat L, De Seta F, Pirulli D, Fabris A, Morgutti M, Crovella S
Am J Reprod Immunol. 2008 Feb;59(2):146-51

Problem: Mannose-binding lectin (MBL) is an important component of the innate immunity, present at the mucosal level in vagina: a common pathogen's entry point. Method of study: We used a rapid genotyping method based on melting temperature assay to search for three single nucleotide polymorphisms (SNPs) located in the first exon of the MBL2 gene and we also measured MBL serum levels in patients with recurrent bacterial vaginosis (rBV) and recurrent vulvovaginal candidiasis (rVVC). Results: Detected frequencies of MBL2 SNPs were comparable to the ones already reported for the Italian population and no significant differences were found between rVVC, rBV and controls. MBL serum levels did not show significant differences between the studied groups. Conclusion: No correlation for the screened mutations has been found neither in protecting nor in favoring the infection in rVVC and rBV patients. Our data demonstrate a lack of association between functional polymorphisms in the first exon of MBL2 gene, MBL deficiency,VVC and rBV.

Vaginal allergic response in women with vulvovaginal candidiasis.
Fan SR, Liao QP, Liu XP, Liu ZH, Zhang D
Int J Gynaecol Obstet. 2008 Feb 14 [Epub ahead of print]

Objective: To determine the concentration of certain cytokines and immunoglobulin (Ig) E in the vaginal lavage fluid (VLF) of women with vulvovaginal candidiasis (VVC). Method: Cytokin and IgE concentrations were measured in the VLF of women with VVC; women free of any genital infections acted as controls. Result: The VLF concentrations of interleukin (IL)-2, IL-8, and interferon (INF)-gamma were higher among women with VVC than in the control group; women with severe VVC had a higher VLF concentration of IL-4 than those with mild to moderate VVC; women with cured VVC had a higher VLF concentration of IL-13 than did controls; and women with VVC or cured VVC had a higher VLF concentration of IgE than did controls ($P<0.05$ for all). Conclusion: Both helper T cells type 1 and innate response cytokines were shown to play a dominant role in the pathogenesis of VVC. This allergic vaginal response in women with VVC suggests that the form of treatment for VVC should be reconsidered.

Basic Science

Spinal neurons activated in response to pudendal or pelvic nerve stimulation in female rats.
Wiedey J, Alexander MS, Marson L
Brain Res.2008 Mar 4;1197:106-14. Epub 2008 Jan 12

The overlapping distribution of spinal neurons activated with either pudendal sensory nerve or pelvic nerve stimulation was examined in the female rat using c-fos immunohistochemistry. Pudendal sensory nerve stimulation resulted in a significant increase in fos-positive cells in the ipsilateral dorsal horn and bilaterally in the medial, lateral and intermediate gray of L5-S1. Pelvic nerve stimulation resulted in significant increases of c-fos immunoreactive nuclei in the ipsilateral dorsal horn, lateral and intermediate gray and bilaterally in the medial gray of L5-S1. Co-distribution of fos immunoreactive nuclei with the

vesicular glutamate transporters (VGlut2 and VGlut3) and neurokinin I receptors were found in distinct regions of the dorsal horn, medial and lateral gray. Specific areas in the medial dorsal horn, dorsal gray commissure, laminae VI and X and dorsal lateral gray were activated after stimulation of the pudendal sensory and pelvic nerves, suggesting these areas contain spinal neurons that receive both somatomotor and visceral inputs and are part of the intraspinal circuit that regulates sexual and voiding function.