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Feature Article

The Evidence-based Vulvodynia Assessment Project. A National Registry for the Study of Vulvodynia.

Lamvu G, Nguyen RH, Burrows LJ, Rapkin A, Witzeman K, Marvel RP, Hutchins D, Witkin SS, Veasley C, Fillingim R, Zolnoun D.

J Reprod Med. 2015 May-Jun;60(5-6):223-35.
http://www.ncbi.nlm.nih.gov/pubmed/26126308

OBJECTIVE: To create a national registry for the study of vulvodynia in order to enhance classification of vulvodynia based on multiple phenotypic domains such as pain characteristics, clinical examination, sexual function, psychological functioning, and distress. **STUDY DESIGN:** Methodology for this prospective cohort registry was institutional review board approved and implemented at 8 enrollment sites starting in 2009. Women underwent gynecologic evaluation and pressure sensory testing for assessment of pain sensitivity in the vaginal mucosa and vaginal muscles. Psychometric questionnaires were used to assess self-described pain, distress, sexual function, and quality of life. **RESULTS:** More than 300 women were enrolled and 176 charts were analyzed. This cohort had a median age of 29 years and median pain duration of 25.5 months. A total of 84% of participants were previously or currently sexually active in spite of pain. The most common pain comorbidities reported by the women were migraines (34%), chronic pelvic pain (22%), and irritable bowel syndrome (20%). Anxiety affected 41% of the cohort. More than 90% presented with localized vestibular pain, and 90% had muscular examination abnormalities. **CONCLUSION:** A national registry for the study of vulvodynia was established with successful enrollment of participants at 8 sites. In addition to the cotton swab evaluation for vulvar allodynia, women with vulvar chronic pain should also be routinely screened for musculoskeletal dysfunction, emotional distress with specific emphasis on anxiety, and comorbid pain conditions.

Vulvodynia/Vulvovaginal Pain

Clitorodynia: A Descriptive Study of Clitoral Pain.
Parada M, D'Amours T, Amsel R, Pink L, Gordon A, Binik YM.
J Sex Med. 2015 Jun 23. doi: 10.1111/jsm.12934.
http://www.ncbi.nlm.nih.gov/pubmed/26104318

INTRODUCTION: Clitorodynia is classified as a type of localized vulvodynia. Our knowledge of this problem is limited to case studies and one published report. **AIMS:** The objective of the present study was to describe quantitatively the clinical characteristics of clitoral pain, to assess interference with sexual function, and to investigate whether clitoral pain is a unitary category. **METHODS:** One hundred twenty-six women with clitoral pain completed an online questionnaire that assessed demographic information, descriptive pain characteristics, intensity and impact on daily activities, sexual function, and gynecological and medical histories. **MAIN OUTCOME MEASURES:** The main outcome measures used for the study are the following: clitoral pain characteristics (e.g., intensity, duration, quality, distress, etc.), short-form McGill pain questionnaire-2, and the female sexual function index. **RESULTS:** Clitoral pain is characterized by frequent and intense pain episodes that can either be provoked or unprovoked, and causes significant impairment in both daily and sexual function. The pain can be localized to the clitoris only or can occur with other genital pain. Comorbidity with other chronic pain disorders is common. A cluster analysis suggested two distinct patterns of clitoral pain, one localized and one generalized. **CONCLUSION:** Our findings indicate that women with clitoral pain suffer from significant, distressing, and often long-term pain, which interferes with sexual and daily activities. Two subtypes of clitoral pain may exist, each with distinct pain characteristics and subjective experiences.

Mucosal versus muscle pain sensitivity in provoked vestibulodynia
Kathryn Witzeman, Ruby HN Nguyen, Alisa Eanes, Sawsan As-Sanie, and Denniz Zolnoun
J Pain Res. 2015; 8: 549–555. Published online 2015 Aug 12. doi: 10.2147/JPR.S85705
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4540214/

Background: An estimated 8.3%—16% of women experience vulvovaginal discomfort during their lifetime. Frequently these patients report provoked pain on contact or with attempted intercourse, commonly referred to as provoked vestibulodynia (PVD). Despite the burden of this condition, little is known about its potential etiologies including pelvic floor muscular dysfunction and mucosal components. This knowledge would be beneficial in developing targeted therapies including physical therapy. **Objective:** To explore the relative contribution of mucosal versus muscle pain sensitivity on pain report from intercourse among women with PVD. **Design:** In this proof of concept study, 54 women with PVD underwent a structured examination assessing mucosal and pelvic muscle sensitivity. **Methods:** We examined three mucosal sites in the upper and lower vestibule. Patients were asked to rate their pain on cotton swab palpation of the mucosa using a 10-point visual analog scale. Muscle pain was assessed using transvaginal application of pressure on right and left puborectalis, and the perineal muscle complex. The Gracely pain scale (0–100) was used to assess the severity of pain with intercourse, with women rating the lowest, average, and highest pain levels; a 100 rating the highest level of pain. **Results:** The lower vestibule's mucosa 5.81 (standard deviation =2.83) was significantly more sensitive than the upper vestibule 2.52 (standard deviation =2.6) (P<0.01) on exam. However, mucosal sensitivity was not associated with intercourse pain, while muscle sensitivity was moderately associated with both average and highest intensity of intercourse pain (r=−0.46, P=0.01 and r=−0.42, P=0.02), respectively.

Conclusion: This preliminary study suggests that mucosal measures alone may not sufficiently capture the spectrum of clinical pain report in women with PVD, which is consistent with the empirical success of physical therapy in this population.

Identification of novel mechanisms involved in generating localized vulvodynia pain.
Falsetta ML, Foster DC, Woeller CF, Pollock SJ, Bonham AD, Haidaris CG, Stodgell CJ, Phipps RP.
Am J Obstet Gynecol. 2015 Jul;213(1):38.e1-38.e12. doi: 10.1016/j.ajog.2015.02.002. Epub 2015 Feb 12.
http://www.ncbi.nlm.nih.gov/pubmed/25683963

OBJECTIVE: Our goal was to gain a better understanding of the inflammatory pathways affected during localized vulvodynia, a poorly understood, common, and debilitating condition characterized by chronic pain of the vulvar vestibule. **STUDY DESIGN:** In a control matched study, primary human fibroblast strains were generated from biopsies collected from localized provoked vulvodynia (LPV) cases and from age- and race-matched controls. We then examined intracellular mechanisms by which these fibroblasts recognize pathogenic Candida albicans; >70% of vulvodynia patients report the occurrence of prior chronic Candida infections, which is accompanied by localized inflammation and elevated production of proinflammatory/pain-associated interleukin (IL)-6 and prostaglandin E2 (PGE2). We focused on examining the signaling pathways involved in recognition of yeast components that are present and abundant during chronic infection. **RESULTS:** Dectin-1, a surface receptor that binds C albicans cell wall glucan, was significantly elevated in vestibular vs external vulvar cells (from areas without pain) in both cases and controls, while its abundance was highest in LPV cases. Blocking Dectin-1 signaling significantly reduced pain-associated IL-6 and PGE2 production during the response to C albicans. Furthermore, LPV patient vestibular cells produced inflammatory mediators in response to low numbers of C albicans cells, while external vulvar fibroblasts were nonresponsive. Inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (proinflammatory transcription factor) nearly abrogated IL-6 and PGE2 production induced by C albicans, in keeping with observations that Dectin-1 signals through the nuclear factor kappa-light-chain-enhancer of activated B cells pathway. **CONCLUSION:** These findings implicate that a fibroblast-mediated proinflammatory response to C albicans contributes to the induction of pain in LPV cases. Targeting this response may be an ideal strategy for the development of new vulvodynia therapies.

Presenting symptoms among premenopausal and postmenopausal women with vulvodynia: a case series.
Phillips NA, Brown C, Foster D, Bachour C, Rawlinson L, Wan J, Bachmann G.
Menopause. 2015 Aug 31.
http://www.ncbi.nlm.nih.gov/pubmed/26325083

OBJECTIVE: The aim of the study was to determine whether there are differences in the clinical presentation of symptoms and vulvar pain ratings in postmenopausal women compared with premenopausal women with provoked vestibulodynia (PVD) enrolled in a clinical trial, after correcting for estrogen deficiency. **METHODS:** Questionnaire data were collected from 76 premenopausal and 24 postmenopausal women enrolled in a clinical trial for PVD. The questionnaire obtained information about the presence or absence of vulvar pain, the characteristics of this pain, and information about the women's demographic characteristics and reproductive health history. Participants were clinically confirmed to have PVD by a positive cotton swab test on pelvic examination and either absence of or corrected vulvovaginal atrophy based on Ratkoff staining with less than 10% parabasal cells. Women

completed a standardized questionnaire describing their vulvar symptoms and rated daily pain on a visual analog scale (0 = no pain to 10 = worse pain imaginable) from sexual intercourse, tampon insertion (as a surrogate measure of intercourse) and 24-hour vulvar pain for 2 weeks during the screening period. Pretreatment data were analyzed before pharmacologic intervention. Chi-square was used to determine differences between pre- and postmenopausal women in demographic characteristics and clinical presentation, and independent t tests were used to analyze pain ratings by (0-10) numeric rating scale (NRS). **RESULTS:** The average ages of premenopausal and postmenopausal women were (30.6 ± 8.6 y) and (54.4 ± 6.5 y), respectively. The groups significantly differed with regard to relationship status (P = 0.002) and race (P = 0.03), but did not differ in years of education (P = 0.49), income level (P = 0.29), or duration of symptoms (P = 0.09). Postmenopausal women reported significantly more vulvar burning (70.00% vs 43.42%, P = 0.03), but there were no differences in vulvar itching (20.00% vs 22.37%, P = 0.82), vulvar stinging (40.00% vs 36.84%, P = 0.79), vulvar aching (50.00% vs 63.16%, P = 0.28), and vulvar stabbing (60.00% vs 71.06% P = 0.34) or in mean number of symptoms (2.40 ± 1.0 vs 2.37 ± 1.4, P = 0.92). Of the 70 participants completing diaries and meeting tampon insertion pain, there were no significant differences in mean (±SD) NRS pain ratings of postmenopausal compared with premenopausal women for tampon insertion (5.66 ± 1.93 vs 5.83 ± 2.15, P = 0.77), daily vulvar pain (3.20 ± 2.55 vs 3.83 ± 2.49, P = 0.38) and sexual intercourse (6.00 ± 2.53 vs 5.98 ± 2.29, P = 0.98). **CONCLUSIONS:** Pre- and postmenopausal women with PVD have similar pain scores, and with the exception of a higher incidence of burning in postmenopausal women, similar presenting clinical symptoms. The statistical power of this conclusion is limited by the small number of postmenopausal women in the study. Further research on the vulvar pain experience of the older woman with PVD is warranted.

Acceptance of vulvovaginal pain in women with provoked vestibulodynia and their partners: associations with pain, psychological, and sexual adjustment.
Boerner KE, Rosen NO.
J Sex Med. 2015 Jun;12(6):1450-62. doi: 10.1111/jsm.12889. Epub 2015 Apr 13.
http://www.ncbi.nlm.nih.gov/pubmed/25869256

INTRODUCTION: Provoked vestibulodynia (PVD) is a common vulvovaginal pain condition associated with negative psychological and sexual consequences for affected women and their sexual partners. Greater pain acceptance has been found to be associated with better functional and psychological outcomes in individuals with chronic pain, and acceptance-based strategies are being increasingly incorporated into treatment protocols. The present study is a novel investigation of pain acceptance in PVD couples. **AIM:** The aim was to examine the associations between acceptance of vulvovaginal pain and women's pain during intercourse, as well as the psychological and sexual adjustment of both women with PVD and their partners. **METHODS:** Sixty-one couples (Mage for women = 27.95 years, SD = 5.87; Mage for men = 30.48 years, SD = 6.70) in which the woman was diagnosed with PVD completed the Chronic Pain Acceptance Questionnaire, in reference to women's vulvovaginal pain. Women also rated their pain during intercourse, and couples completed measures of anxiety, depression, sexual function, and sexual satisfaction. **MAIN OUTCOME MEASURES:** Dependent measures were (i) women's self-reported pain during intercourse on a numerical rating scale; (ii) State-Trait Anxiety Inventory trait subscale; (iii) Beck Depression Inventory-II; (iv) Derogatis Interview for Sexual Functioning; and (v) Global Measure of Sexual Satisfaction Scale. **RESULTS:** Women's greater pain acceptance was associated with their lower self-reported pain during intercourse, controlling for partner's pain acceptance. Greater pain acceptance among women was associated with their own lower anxiety and depression, greater sexual functioning, as well as their own and their partner's greater

sexual satisfaction, controlling for the partner's pain acceptance. Additionally, greater pain acceptance among male partners was associated with their own lower depression. **CONCLUSIONS:** Findings suggest that psychological interventions for PVD should target increasing couples' vulvovaginal pain acceptance in order to improve women's pain and the sexual and psychological functioning of both members of the couple.

Depression and Posttraumatic Stress Disorder Among Women with Vulvodynia: Evidence from the Population-Based Woman to Woman Health Study.
Iglesias-Rios L, Harlow SD, Reed BD.
J Womens Health (Larchmt). 2015 Jul;24(7):557-62. doi: 10.1089/jwh.2014.5001. Epub 2015 May 7.
http://www.ncbi.nlm.nih.gov/pubmed/25950702

BACKGROUND: Psychological disorders may affect the pain experience of women with vulvodynia, but evidence remains limited. The present study aimed to describe the magnitude of the association of depression and posttraumautic stress disorder (PTSD) with the presence of vulvodynia in a nonclinical population from southeastern Michigan. **METHODS:** Baseline data from 1,795 women participating in the Woman to Woman Health Study, a multiethnic population-based study, was used for this analysis. Validated screening questionnaires were conducted to assess vulvodynia, depression, and PTSD. Modified Poisson regression models with a robust variance estimation were used to estimate prevalence ratios (PR) and their 95% confidence intervals (CI) for the association between vulvodynia status and two mental health conditions, depression and PTSD. **RESULTS:** In the adjusted models, women who screened positive for depression had a 53% higher prevalence of having vulvodynia (PR=1.53; 95% CI: 1.12, 2.10) compared with women who screened negative for depression. Women who screened positive for PTSD had more than a two-fold increase in the prevalence of having vulvodynia (PR=2.37; 95% CI: 1.07, 5.25) compared with women who screened negative for PTSD. **CONCLUSIONS:** The increased prevalence of vulvodynia among those screening positive for depression or PTSD suggests that these disorders may contribute to the likelihood of reporting vulvodynia. Alternatively, vulvodynia, depression, and PTSD may have a common pathophysiological and risk profile. Prospective studies are needed to improve our understanding of the temporal relation between mental health conditions and vulvar pain.

Vulvodynia and Concomitant Femoro-Acetabular Impingement: Long-Term Follow-up After Hip Arthroscopy.
Coady D, Futterman S, Harris D, Coleman SH.
J Low Genit Tract Dis. 2015 Jul;19(3):253-6. doi: 10.1097/LGT.0000000000000108.
http://www.ncbi.nlm.nih.gov/pubmed/25853634

OBJECTIVE: We hypothesized that in patients with vulvodynia and femoro-acetabular impingement (FAI), vulvar pain may be generated by the effect of FAI on pelvic floor structures, and treatment with arthroscopy may improve vulvodynia. We also sought to identify characteristics of patients whose vulvodynia improved after arthroscopy. **MATERIALS AND METHODS:** A case series of patients with vulvodynia and FAI underwent physical therapy, and, if hip symptoms did not improve, arthroscopy. Three to 5 years postoperatively, follow-up of outcomes after arthroscopy on vulvodynia was performed using chart review and patient questionnaire. Clinical characteristics and pain scores describing patients with and without vulvodynia improvement were assessed. **RESULTS:** Twenty-six patients with generalized unprovoked vulvodynia (GUV) or clitorodynia underwent arthroscopy for FAI. Six patients,

all younger than 30 years, experienced lasting improvement in vulvodynia. Twenty patients, with an older mean age, longer mean vulvodynia duration, and mainly severe pain scores, did not experience vulvar pain improvement after arthroscopy. **CONCLUSION:** This case series describes improved vulvodynia outcomes after arthroscopy for FAI in women younger than 30 years. Patients with vulvar pain and coexisting FAI had GUV and clitorodynia.

Are primary and secondary provoked vestibulodynia two different entities? A comparison of pain, psychosocial, and sexual characteristics.
Aerts L, Bergeron S, Corsini-Munt S, Steben M, Pâquet M.
J Sex Med. 2015 Jun;12(6):1463-73. doi: 10.1111/jsm.12907. Epub 2015 May 11.
http://www.ncbi.nlm.nih.gov/pubmed/25963291

INTRODUCTION: Provoked vestibulodynia (PVD) is suspected to be the most frequent cause of vulvodynia in premenopausal women. Based on the onset of PVD relative to the start of sexual experience, PVD can be divided into primary (PVD1) and secondary PVD (PVD2). Studies comparing these PVD subgroups are inconclusive as to whether differences exist in sexual and psychosocial functioning. **AIM:** The aim of this study was to compare the pain, sexual and psychosocial functioning of a large clinical and community-based sample of premenopausal women with PVD1 and PVD2. **METHODS:** A total of 269 women (n = 94 PVD1; n = 175 PVD2) completed measures on sociodemographics, pain, sexual, and psychosocial functioning. **MAIN OUTCOME MEASURES:** Dependent variables were the 0-10 pain numerical rating scale, McGill-Melzack Pain Questionnaire, Female Sexual Function Index, Global Measure of Sexual Satisfaction, Beck Depression Inventory-II, Painful Intercourse Self-Efficacy Scale, Pain Catastrophizing Scale, State-Trait Anxiety Inventory Trait Subscale, Ambivalence over Emotional Expression Questionnaire, Hurlbert Index of Sexual Assertiveness, Experiences in Close Relationships Scale-Revised, and Dyadic Adjustment Scale-Revised. **RESULTS:** At first sexual relationship, women with PVD2 were significantly younger than women with PVD1 ($P < 0.01$). The average relationship duration was significantly longer in women with PVD2 compared with women with PVD1 ($P < 0.01$). Although women with PVD1 described a significantly longer duration of pain compared with women with PVD2 ($P < 0.01$), no significant subtype differences were found in pain intensity during intercourse. When controlling for the sociodemographics mentioned earlier, no significant differences were found in sexual, psychological, and relational functioning between the PVD subgroups. Nevertheless, on average, both groups were in the clinical range of sexual dysfunction and reported impaired psychological functioning. **CONCLUSIONS:** The findings show that there are no significant differences in the sexual and psychosocial profiles of women with PVD1 and PVD2. Results suggest that similar psychosocial and sex therapy interventions should be offered to both subgroups of PVD.

History of Abuse in Women With Vulvar Pruritus, Vulvodynia, and Asymptomatic Controls.
Cohen-Sacher B, Haefner HK, Dalton VK, Berger MB.
J Low Genit Tract Dis. 2015 Jul;19(3):248-52. doi: 10.1097/LGT.0000000000000075.
http://www.ncbi.nlm.nih.gov/pubmed/26111040

OBJECTIVE: Chronic vulvar pruritus and vulvodynia are common vulvar diseases. The aim of this study was to compare gynecologic and sexual and physical abuse histories from patients with these diagnoses and from healthy controls. **MATERIALS AND METHODS:** Questionnaires were self-completed by patients diagnosed with vulvar itch-scratch (n = 93), patients diagnosed with vulvodynia (n = 232), and patients

presenting for annual gynecologic examinations (n = 104) at the University of Michigan Hospitals, Ann Arbor, MI. **RESULTS:** Patients who came for annual examinations were less likely to report past gynecologic infections ($p < .05$) and indicated higher interest in and more frequent sexual activity than the other 2 groups ($p = .003$). Vulvodynia patients had the highest scores on the McGill Pain Questionnaire ($p < .001$). Subjects with either vulvar disorder were more likely to self-report a history of gynecologic infections than annual examination controls. Rates of sexual ($p = .78$) and physical abuse ($p = .12$) were similar for all 3 groups. **CONCLUSIONS:** Patients with vulvar pruritus and vulvodynia report similar rates of sexual and physical abuse.

Vulvodynia: The Role of Inflammation in the Etiology of Localized Provoked Pain of the Vulvar Vestibule (Vestibulodynia).
Akopians AL, Rapkin AJ.
Semin Reprod Med. 2015 Jul;33(4):239-45. doi: 10.1055/s-0035-1554919. Epub 2015 Jul 1.
http://www.ncbi.nlm.nih.gov/pubmed/26132928

Vulvar pain affecting the vestibule (vestibulodynia) is an enigmatic pain disorder that greatly affects quality of life and sexual functioning. The most common form of the disorder (localized provoked vulvodynia) is initiated by genital contact but is otherwise asymptomatic. Findings on examination are limited to excessive tenderness of the vestibule with light touch with cotton swab but may also include localized erythema and pelvic floor muscle tightness and tenderness. This review will summarize the literature regarding the role of inflammation in the genesis of the disorder. Some evidence exists for altered histology consisting of increased numbers of mast cells and nerve endings. Immunological abnormalities that have been reported include altered cytokines and neurokines. Abnormal inflammatory response and heightened sensitivity of the vaginal opening has been documented in a murine model of vaginal infection with Candida albicans. In vitro studies of fibroblasts from the vestibule of affected women with vestibulodynia demonstrate a proinflammatory response to C albicans that may be important in the initiation of pain. However, thus far none of the findings have led to adequate treatments.

Current concepts in vulvodynia with a focus on pathogenesis and pain mechanisms.
Thornton AM, Drummond C.
Australas J Dermatol. 2015 Jul 6. doi: 10.1111/ajd.12365.
http://www.ncbi.nlm.nih.gov/pubmed/26148424

Vulvodynia is a common and debilitating chronic pain syndrome characterised by neuropathic-type pain. Localised provoked vulvodynia is the most common type, followed by generalised unprovoked vulvodynia. Vulvodynia is a diagnosis of exclusion. The cause is unknown but current research suggests an underlying predisposition to increased sensitivity to pain and peripheral and central neural sensitisation. Musculoskeletal factors also play an important role. Vulvodynia has a significant impact on the quality of life, mood, functional ability and relationships of patients and their partners. It is highly associated with anxiety and depression. Treatment needs to follow a biopsychosocial model and be tailored to the patient. A multimodal and multidisciplinary approach is often most effective. We have suggested a therapeutic ladder.

Approach and Avoidance Sexual Goals in Couples with Provoked Vestibulodynia: Associations with Sexual, Relational, and Psychological Well-Being.
Rosen NO, Muise A, Bergeron S, Impett EA, Boudreau GK.
J Sex Med. 2015 Jul 14. doi: 10.1111/jsm.12948.
http://www.ncbi.nlm.nih.gov/pubmed/26176989

INTRODUCTION: Provoked vestibulodynia (PVD) is a prevalent vulvovaginal pain condition that is triggered primarily during sexual intercourse. PVD adversely impacts women's and their partners' sexual relationship and psychological well-being. Over 80% of women with PVD continue to have intercourse, possibly because of sexual goals that include wanting to pursue desirable outcomes (i.e., approach goals; such as a desire to maintain intimacy) and avoid negative outcomes (i.e., avoidance goals; such as avoiding a partner's disappointment). **AIM:** The aim of this study was to investigate associations between approach and avoidance sexual goals and women's pain, as well as the sexual, relational, and psychological well-being of affected couples. **METHODS:** Women with PVD (N = 107) and their partners completed measures of sexual goals, sexual satisfaction, relationship satisfaction, and depression. Women also completed measures of pain during intercourse and sexual functioning. **MAIN OUTCOME MEASURES:** (1) Global Measure of Sexual Satisfaction Scale, (2) Dyadic Adjustment Scale-Revised or the Couple Satisfaction Index, (3) Beck Depression Inventory-II, (4) numerical rating scale of pain during intercourse, and (5) Female Sexual Function Index. **RESULTS:** When women reported higher avoidance sexual goals, they reported lower sexual and relationship satisfaction, and higher levels of depressive symptoms. In addition, when partners of women reported higher avoidance sexual goals, they reported lower relationship satisfaction. When women reported higher approach sexual goals, they also reported higher sexual and relationship satisfaction. **CONCLUSIONS:** Targeting approach and avoidance sexual goals could enhance the quality and efficacy of psychological couple interventions for women with PVD and their partners.

Is the 2003 ISSVD terminology and classification of vulvodynia up-to-date? A neurobiological perspective.
Micheletti L, Radici G, Lynch PJ.
J Obstet Gynaecol. 2015 Jun 17:1-5.
http://www.ncbi.nlm.nih.gov/pubmed/26082295

This paper aims to determine if the 2003 International Society for the Study of Vulvovaginal Disease (ISSVD) terminology and classification of vulval pain is up-to-date, according to a current and widely accepted neurobiological pain classification, which divides pain into nociceptive, inflammatory and pathological pain with the latter subdivided into neuropathic and dysfunctional pain. Nociceptive pain is protective, adaptive, high-threshold pain provoked by noxious stimuli. Inflammatory pain is protective, adaptive, low-threshold pain associated with peripheral tissue damage and inflammation. Pathological pain is non-protective, maladaptive, low-threshold pain caused by structural damage to the nervous system (neuropathic pain) or by its abnormal function (dysfunctional pain). The 2003 ISSVD vulval pain classification should be revised in terms of current neurobiological pain information. Inflammatory vulval pain occurs as a result of specific infectious, inflammatory and neoplastic disorders. Neuropathic vulval pain arises following a specific neurological disorder, responsible for structural damage to the nervous system. Vulvodynia is dysfunctional vulval pain, caused by abnormal function of the nervous system itself.

Vulvodynia.
Hoffstetter S, Shah M.
Clin Obstet Gynecol. 2015 Jun 24.
http://www.ncbi.nlm.nih.gov/pubmed/26125963

Vulvodynia, a chronic pain disorder, affects women throughout the lifespan. Appropriate evaluation and diagnosis is necessary to enable effective management. The etiology is considered multifactorial. Therapies include self-management, nonpharmacologic, pharmacologic, and surgical. Vulvodynia can have a significant impact upon a patient's quality of life. Emotional and psychological support is invaluable. This article serves to give the primary gynecologist and practitioner a basic framework with which to identify, diagnose, and begin treatment for such patients as well as understanding for referral if necessary. The initial evaluation and physical examination will be discussed in detail.

MicroRNA expression profiles differentiate chronic pain condition subtypes.
Ciszek BP, Khan AA, Dang H, Slade GD, Smith S, Bair E, Maixner W, Zolnoun D, Nackley AG.
Transl Res. 2015 Jun 24. pii: S1931-5244(15)00213-3. doi: 10.1016/j.trsl.2015.06.008.
http://www.ncbi.nlm.nih.gov/pubmed/26166255

Chronic pain is a significant health care problem, ineffectively treated because of its unclear etiology and heterogeneous clinical presentation. Emerging evidence demonstrates that microRNAs (miRNAs) regulate the expression of pain-relevant genes, yet little is known about their role in chronic pain. Here, we evaluate the relationship among pain, psychological characteristics, plasma cytokines, and whole blood miRNAs in 22 healthy controls (HCs); 33 subjects with chronic pelvic pain (vestibulodynia, VBD); and 23 subjects with VBD and irritable bowel syndrome (VBD + IBS). VBD subjects were similar to HCs in self-reported pain, psychological profiles, and remote bodily pain. VBD + IBS subjects reported decreased health and function; and an increase in headaches, somatization, and remote bodily pain. Furthermore, VBD subjects exhibited a balance in proinflammatory and anti-inflammatory cytokines, whereas VBD + IBS subjects failed to exhibit a compensatory increase in anti-inflammatory cytokines. VBD subjects differed from controls in expression of 10 miRNAs of predicted importance for pain and estrogen signaling. VBD + IBS subjects differed from controls in expression of 11 miRNAs of predicted importance for pain, cell physiology, and insulin signaling. miRNA expression was correlated with pain-relevant phenotypes and cytokine levels. These results suggest that miRNAs represent a valuable tool for differentiating VBD subtypes (localized pain with apparent peripheral neurosensory disruption vs widespread pain with a central sensory contribution) that may require different treatment approaches.

Comorbid Disorders

Genital and sexual pain in women.
Graziottin A, Gambini D, Bertolasi L.
Handb Clin Neurol. 2015;130:395-412. doi: 10.1016/B978-0-444-63247-0.00023-7.
http://www.ncbi.nlm.nih.gov/pubmed/26003257

This chapter discusses the all too common problem of sex-related pain in women. Pain is a complex perceptive experience, involving biologic as well as psychologic and relational meanings. They become increasingly important with the chronicity of pain. Neurologists are quite aware of the painful aspect of

many neurologic disorders, but lifelong and acquired genital and sexual pain is still neglected in a consistent percentage of women. One reason is the view - still held by many - that psychologic factors play the most important role in sex-related pain complaints. The consequences of diagnostic delay can be dramatic. Persisting tissue inflammation induces pain to change from acute and "nociceptive," which indicates a "friendly signal," alerting one to ongoing tissue damage, to chronic and "neuropathic," a disease per se. Whilst the primary disease is progressing and neuroinflammation becomes a prominent feature, affected women have to bear years of pain and distress, huge quantifiable and non-quantifiable costs, and a progressive deterioration of personal and relational health and happiness. The scenario is even more dramatic when pain complicates an already disabling disease. The main aspects considered in this chapter include neuroinflammation as a key feature of pain; genital and sexual pain as part of neurologic diseases; and genital and sexual pain syndrome (dyspareunia and vaginismus) as primary problems, and their pelvic comorbidities (bladder pain syndrome, endometriosis, irritable bowel syndrome, provoked vestibulodynia/vulvodynia). Finally, we discuss iatrogenic pain, i.e., genital and sexual pain caused by ill-conceived medical, surgical, pharmacologic or radiologic therapeutic interventions.

Dermatological Disorders/Infectious Disease

A retrospective analysis of pediatric patients with lichen sclerosus treated with a standard protocol of class I topical corticosteroid and topical calcineurin inhibitor.
Anderson K, Ascanio NM, Kinney MA, Krowchuk DP, Jorizzo JL.
J Dermatolog Treat. 2015 Jul 3:1-3. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/26138407

BACKGROUND: Lichen sclerosus (LS) is a chronic, inflammatory condition of the skin, affecting primarily the anogenital region potentially leading to changes in vaginal architecture and vulvar squamous cell carcinoma. Current recommended treatment for LS is high-potency corticosteroids. Calcineurin inhibitors may also have a role. **OBJECTIVE:** The objective of this study is to introduce a treatment regimen involving clobetasol to induce remission, then tacrolimus to maintain remission in pediatric females with LS. **METHODS:** As a retrospective case series, we report 14 pediatric females between 2 and 10 years of age with LS treated with clobetasol 0.05% topical ointment and systematically bridged to tacrolimus 0.1% topical ointment. For each patient, gender, age at disease onset, and clinical symptoms and features were noted. Time in weeks to 75% clearance and to complete clearance were recorded. **RESULTS:** Thirteen patients showed complete clearance. One patient showed significant clearance of the disease. The time to complete clearance averaged 43.1 weeks, with a range of 4-156 weeks. **CONCLUSIONS:** The use clobetasol to induce remission and tacrolimus to maintain remission can be used to treat LS in pediatric females. This regimen may minimize side effects associated with long-term, high-potency corticosteroid use and reduce the risk of changes to genital architecture secondary to LS.

Inflammatory Vulvar Dermatoses.
Guerrero A, Venkatesan A.
Clin Obstet Gynecol. 2015 Jun 24.
http://www.ncbi.nlm.nih.gov/pubmed/26125955

Inflammatory vulvar dermatoses affect many women, but are likely underdiagnosed due to embarrassment and reluctance to visit a health care provider. Although itch and pain are common presenting symptoms, the physical examination can help distinguish between different disease entities. Because many women's health providers have minimal training in the categorization and management of dermatologic disease, definitive diagnosis and management can be difficult. Herein, strategies for diagnosing vulvar lichen sclerosus, lichen planus, contact dermatitis, lichen simplex chronicus, and psoriasis are discussed along with basic management of these diseases, which commonly involves decreasing inflammation through behavioral change, gentle skin care, topical corticosteroids, and systemic therapies.

Long-term Management of Adult Vulvar Lichen Sclerosus: A Prospective Cohort Study of 507 Women.
Lee A, Bradford J, Fischer G.
JAMA Dermatol. 2015 Jun 12. doi: 10.1001/jamadermatol.2015.0643.
http://www.ncbi.nlm.nih.gov/pubmed/26070005

Importance: Adult vulvar lichen sclerosis (VLS) may be complicated by loss of vulvar structure and vulvar carcinoma. There is a lack of evidence as to the ideal method to maintain long-term remission and prevent complications. **Objectives:** To determine whether long-term preventive topical corticosteroid (TCS) treatment of VLS, with a target outcome of induction and maintenance of normal skin texture and color, reduces the risk of vulvar carcinoma, relieves symptoms, improves function, and preserves vulvar architecture, and to evaluate the adverse effects of treatment. **Design, Setting, and Participants:** A prospective longitudinal cohort study was conducted in 507 women with biopsy-proved VLS from January 2, 2008, through September 26, 2014, in the private practice of a dermatologist and a gynecologist in Sydney, Australia. **Interventions:** Preventive treatment using TCSs of various potencies, adjusted to meet a target outcome of normal skin color and texture, with regular long-term follow-up by a dermatologist or gynecologist. **Main Outcomes and Measures:** Symptoms or signs of VLS, scarring, development of malignant neoplasms, and adverse effects. **Results:** The mean age at presentation was 55.4 years (range, 18-86 years); duration of symptoms at presentation, 5.0 years (range, 0.1-40.0 years); and duration of follow-up, 4.7 years (range, 2.0-6.8 years). Remission was induced with a potent TCS, followed by regular preventive TCS treatment of a potency titrated to achieve the target outcome. Patients were followed up at least annually. A total of 150 patients (29.6%) did not carry out the advised treatment and were considered partially compliant. A total of 357 patients (70.4%) adhered to treatment instructions and were considered compliant. Biopsy-proved squamous cell carcinoma or vulvar intraepithelial neoplasia occurred during follow-up in 0 of the compliant patients vs 7 (4.7%) of the partially compliant patients ($P < .001$). Suppression of symptoms occurred in 333 (93.3%) compliant patients vs 87 (58.0%) partially compliant patients ($P < .001$). Adhesions and scarring occurred during follow-up in 12 (3.4%) compliant patients and 60 (40.0%) partially compliant patients ($P < .001$). Reversible TCS-induced cutaneous atrophy occurred in 4 (1.1%) compliant patients and 3 (2.0%) partially compliant patients. **Conclusions and Relevance:** This prospective, single-center, longitudinal cohort study of adult patients with VLS suggests that individualized preventive TCS regimens that achieve objective normality of skin color and texture and are used by compliant patients who attend regular long-term follow-up visits may modify the course of the disease. There was a significant difference in

symptom control, scarring, and occurrence of vulvar carcinoma between compliant and partially compliant patients. The adverse effects of TCSs were minimal.

Eosinophils in Lichen Sclerosus et Atrophicus.
Keith PJ, Wolz MM, Peters MS.
J Cutan Pathol. 2015 Jul 8. doi: 10.1111/cup.12556.
http://www.ncbi.nlm.nih.gov/pubmed/26152335

BACKGROUND: The classic histopathologic features of lichen sclerosus et atrophicus (LS) include lymphoplasmacytic inflammation below a zone of dermal edema and sclerosis. The presence of eosinophils in LS has received little attention, but the finding of tissue eosinophils, particularly eosinophilic spongiosis in LS, has been suggested as a marker for the coexistence of autoimmune bullous disease or allergic contact dermatitis (or both). We sought to determine whether the histopathologic presence of dermal eosinophils or eosinophilic spongiosis (or both) in biopsies from patients with LS is associated with autoimmune bullous disease, autoimmune connective tissue disease, or allergic contact dermatitis. **METHODS:** A retrospective review was performed of the histopathology and medical records of 235 patients with LS who were evaluated from June 1992 to June 2012. **RESULTS:** Sixty-nine patients (29%) had eosinophils on histopathology. Among patients with associated diseases, a statistically significant association between the eosinophil cohort and the cohort without eosinophils was not detected. **CONCLUSIONS:** The importance of eosinophils is uncertain, but our data suggest that the finding of tissue eosinophils alone is not sufficient to prompt an extensive workup for additional diagnosis.

Evidence-based (S3) Guideline on (anogenital) Lichen sclerosus.
Kirtschig G, Becker K, Günthert A, Jasaitiene D, Cooper S, Chi CC, Kreuter A, Rall KK, Aberer W, Riechardt S, Casabona F, Powell J, Brackenbury F, Erdmann R, Lazzeri M, Barbagli G, Wojnarowska F.
J Eur Acad Dermatol Venereol. 2015 Jul 22. doi: 10.1111/jdv.13136.
http://www.ncbi.nlm.nih.gov/pubmed/26202852

Lichen sclerosus (LS) is an inflammatory skin disease that usually involves the anogenital area. All patients with symptoms or signs suspicious of lichen sclerosus should be seen at least once initially by a physician with a special interest in the disease in order to avoid delay in diagnosis, as early treatment may cure the disease in some and reduce or prevent scarring. The diagnosis is made clinically in most cases. Biopsies should only be performed under certain circumstances. The gold standard for treatment remains potent to very potent topical steroids; however, mild and moderate disease in boys and men may be cured by circumcision. Certain triggers should be avoided.
http://www.euroderm.org/edf/index.php/edf-guidelines/category/5-guidelines-miscellaneous

Non-albicans Candida Vulvovaginitis: Treatment Experience at a Tertiary Care Vaginitis Center.
Powell AM, Gracely E, Nyirjesy P.
J Low Genit Tract Dis. 2015 Jun 16.
http://www.ncbi.nlm.nih.gov/pubmed/26083330

OBJECTIVES: The aims of this study are to analyze a cohort of women with vulvovaginal symptoms and positive cultures for non-albicans Candida (NAC) to determine whether yeast was responsible for their symptoms and to evaluate the mycological effectiveness of various regimens. **METHODS:** This observational study was performed from retrospective chart review of patients with positive NAC cultures between April 1, 2008, and January 31, 2011, at a tertiary care vaginitis center. Patient intake demographics were entered into a database. Follow-up visits were analyzed for data about patient treatments and outcomes. Patients were considered a clinical cure if their symptoms were significantly improved and mycologic cure (MC) if later yeast cultures were negative. If clinical symptoms improved at the same time as MC, the isolate was considered the proximate cause for the symptoms. **RESULTS:** One hundred eight patients meeting entry criteria were analyzed. Boric acid was effective at obtaining MC in 32 (78%) of 41 patients with C. glabrata, 3 of 3 patients with C. tropicalis, and 3 of 3 patients with C. lusitaniae. Fluconazole was effective as initial treatment for 3 (60%) of 5 patients with C. glabrata and 13 (81%) of 16 patients with C. parapsilosis. In 52.7% of C. glabrata, 66.7% of C. parapsilosis, and 57.1% of C. tropicalis cases, effective antifungal therapy led to symptom improvement. **CONCLUSIONS:** In a tertiary care vaginitis center, NAC, when isolated on culture, caused clinically significant infections in approximately half of symptomatic patients. A majority of infections can be effectively treated with boric acid or fluconazole regardless of the non-albicans Candida species.

The dynamic changes of vaginal microecosystem in patients with recurrent vulvovaginal candidiasis: a retrospective study of 800 patients.
Yue XA, Chen P, Tang Y, Wu X, Hu Z.
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http://www.ncbi.nlm.nih.gov/pubmed/26041326

PURPOSE: Vaginal microecological environment is an important factor of recurrent vulvovaginal candidiasis (RVVC). This study was undertaken to investigate dynamic changes of vaginal microecosystem in patients with RVVC. **METHODS:** Four hundred patients with VVC and 400 healthy women of reproductive age who admitted to the hospital from January 2012 to December 2013 were evaluated retrospectively. Vaginal microecological factors were evaluated before and after treatment until no recurrence, including vaginal cleanliness, white blood cells, Lactobacillus, Lactobacillus classification, bacteria density, flora diversity, Nugent scores, etc. The grouping was done according to the recurrence of the disease. Every time after treatment, the relapsing patients were defined as case group and the cured patients without recurrence were defined as control group. The differences in the results between the case and the control groups were analyzed by t test. **RESULTS:** With the development of RVVC, the ages of all case groups were lower than the corresponding control groups. In different stages of the disease, the bacteria density of the case groups and their corresponding control groups had no significant difference ($P > 0.05$). Most of the microecological indicators of the first occurring group were significantly different ($P < 0.05$) from that of the control group. In the recurrence groups, only a few indicators were significantly different from the control groups. The values of all vaginal microecological indicators (except Lactobacillus) of all case groups were higher than that of the control groups. The values of Lactobacillus of all RVVC case groups were lower than that of the RVVC control groups. **CONCLUSIONS:** There were vaginal microecological imbalances in all developing stages

of RVVC. As for vaginal flora, diverse sorts changed to normal Lactobacillus dominantly with the development of RVVC. In the first occurrence of RVVC, after antifungal treatment, Lactobacillus is suggested to be timely supplemented to restore vaginal microecological balance.

Pain Science

A streptozotocin-induced diabetic neuropathic pain model for static or dynamic mechanical allodynia and vulvodynia: validation using topical and systemic gabapentin.
Ali G, Subhan F, Abbas M, Zeb J, Shahid M, Sewell RD.
Naunyn Schmiedebergs Arch Pharmacol. 2015 Jul 3.
http://www.ncbi.nlm.nih.gov/pubmed/26134846

Neuropathic vulvodynia is a state of vulval discomfort characterized by a burning sensation, diffuse pain, pruritus or rawness with an acute or chronic onset. Diabetes mellitus may cause this type of vulvar pain in several ways, so this study was conducted to evaluate streptozotocin-induced diabetes as a neuropathic pain model for vulvodynia in female rats. The presence of streptozotocin (50 mg/kg i.p.)-induced diabetes was initially verified by disclosure of pancreatic tissue degeneration, blood glucose elevation and body weight loss 5-29 days after a single treatment. Dynamic (shortened paw withdrawal latency to light brushing) and static (diminished von Frey filament threshold pressure) mechanical allodynia was then confirmed on the plantar foot surface. Subsequently, both static and dynamic vulvodynia was detected by application of the paradigm to the vulval region. Systemic gabapentin (75 mg/kg, i.p.) and topical gabapentin (10 % gel) were finally tested against allodynia and vulvodynia. Topical gabapentin and the control gel vehicle significantly increased paw withdrawal threshold in the case of the static allodynia model and also paw withdrawal latency in the model for dynamic allodynia when compared with the streptozotocin-pretreated group. Likewise, in the case of static and dynamic vulvodynia, there was a significant antivulvodynia effect of systemic and topical gabapentin treatment. These outcomes substantiate the value of this model not only for allodynia but also for vulvodynia, and this was corroborated by the findings not only with systemic but also with topical gabapentin.