

# NVA Research Update E- Newsletter

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## Vulvodynia

### Persistent Vulvar Pain

Committee Opinion No. 673. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e78-84.

<http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Gynecologic-Practice/Persistent-Vulvar-Pain>

Persistent vulvar pain is a complex disorder that frequently is frustrating to the patient and the clinician. It can be difficult to treat and rapid resolution is unusual, even with appropriate therapy. Vulvar pain can be caused by a specific disorder or it can be idiopathic. Idiopathic vulvar pain is classified as vulvodynia. Although optimal treatment remains unclear, consider an individualized, multidisciplinary approach to address all physical and emotional aspects possibly attributable to vulvodynia. Specialists who may need to be involved include sexual counselors, clinical psychologists, physical therapists, and pain specialists. Patients may perceive this approach to mean the practitioner does not believe their pain is “real”; thus, it is important to begin any treatment approach with a detailed discussion, including an explanation of the diagnosis and determination of realistic treatment goals. Future research should aim at evaluating a multimodal approach in the treatment of vulvodynia, along with more research on the etiologies of vulvodynia.

### Recruitment methods in a clinical trial of provoked vulvodynia: Predictors of enrollment.

Bachour CC, Bachmann GA, Foster DC, Wan JY, Rawlinson LA, Brown CS, Gabapentin Study Group (GABAgroup).

*Clin Trials*. 2016 Aug 2. pii: 1740774516663461.

<http://www.ncbi.nlm.nih.gov/pubmed/27488223>

**BACKGROUND:** Successful recruitment in clinical trials for chronic pain conditions is challenging, especially in women with provoked vulvodynia due to reluctance in discussing pain associated with sexual intercourse. The most successful recruitment methods and the characteristics of women reached with these methods are unknown. **OBJECTIVE:** To compare the effectiveness and efficiency of four recruitment methods and to determine socioeconomic predictors for successful enrollment in a National Institutes of Health-sponsored multicenter clinical trial evaluating a gabapentin intervention in women with provoked vulvodynia. **METHODS:** Recruitment methods utilized mass mailing, media, clinician referrals and community outreach. Effectiveness (number of participants enrolled) and efficiency (proportion screened who enrolled) were determined. Socioeconomic variables including race, educational level, annual household income, relationship status, age, menopausal status and employment status were also evaluated regarding which recruitment strategies were best at targeting specific cohorts. **RESULTS:** Of 868 potential study participants, 219 were enrolled. The most effective

recruitment method in enrolling participants was mass mailing ( $p < 0.001$ ). There were no statistically significant differences in efficiency between recruitment methods ( $p = 0.11$ ). Relative to clinician referral, black women were 13 times as likely to be enrolled through mass mailing (adjusted odds ratio 12.5, 95% confidence interval, 3.6-43.1) as white women. There were no differences in enrollment according to educational level, annual income, relationship status, age, menopausal status, or employment status and recruitment method. **CONCLUSION:** In this clinical trial, mass mailing was the most effective recruitment method. Race of participants enrolled in a provoked vulvodynia trial was related to the recruitment method.

### **Vestibular Mast Cell Density in Vulvodynia: A Case-Controlled Study.**

Papoutsis D, Haefner HK, Crum CP, Opiari AW Jr, Reed BD.

*J Low Genit Tract Dis.* 2016 Jul;20(3):275-9. doi: 10.1097/LGT.0000000000000221.

<http://www.ncbi.nlm.nih.gov/pubmed/27224531>

**OBJECTIVES:** To identify whether mast cell densities in vulvar biopsies from the vestibule are associated with vulvodynia. **METHODS:** We enrolled 100 women aged 19 to 59 years with confirmed vulvodynia cases, 100 racially matched controls, and 100 black control women. All had vulvar biopsies performed at the 7 o'clock position of the vestibule, which were then immunostained to detect c-KIT protein. The numbers of c-KIT positive mast cells per  $\times 400$  magnification field were manually counted, and t tests and logistic regression were used to assess the association with case-control status. **RESULTS:** Of the biopsies, 235 were adequate samples for c-KIT testing for mast cells. The mast cell density was substantially lower in black control women ( $13.9 \pm 10.9$ ) in comparison to white control women ( $22.5 \pm 13.2$   $p < 0.001$ ): hence the analysis was confined to white cases and racially matched control women. Compared with racially matched controls, cases were younger, more likely to be married, and reported a higher household income. The average number of mast cells per  $\times 400$  magnification field overall was  $19.1 \pm 13.2$  (range, 0-62). There was no difference in the mast cell count between racially matched cases ( $22.4 \pm 13.9$  per  $\times 400$  field) and controls ( $22.5 \pm 13.2$ ) in either the univariate or multivariable analyses. Within the group of cases, there was no difference in mast cell density based on the presence or absence of a variety of urogenital symptoms. **CONCLUSIONS:** No difference in mast cell density in biopsies of the vestibule was found between white cases and racially matched controls. Black control women have a lower mast cell density compared with white control women.

### **What Do Patients Want? A Needs Assessment of Vulvodynia Patients Attending a Vulvar Diseases Clinic.**

LePage K, Selk A.

*Sex Med.* 2016 Jul 30. pii: S2050-1161(16)30046-0. doi: 10.1016/j.esxm.2016.06.003.

<http://www.ncbi.nlm.nih.gov/pubmed/27484917>

**INTRODUCTION:** Vulvodynia is a chronic pain disorder that negatively impacts the quality of life of affected women. **AIM:** The goal of this study was to identify unmet needs among localized provoked vulvodynia patients. **METHODS:** A qualitative needs assessment was performed in a subspecialized vulvar clinic in a single academic institution in Canada. Semistructured interviews were conducted, recorded, and analyzed using the constant comparative method of grounded theory to identify common themes. **MAIN OUTCOME MEASURES:** Interviews were conducted until theme saturation was achieved. **RESULTS:** A diverse sample of 8 patients completed all components of the study. The most prominent unmet needs raised by patients in their interviews were categorized into 3 main themes: (1) challenges

related to obtaining a diagnosis of vulvodynia and finding practitioners who are knowledgeable about vulvodynia; (2) challenges related to the current impact of the disease physically, emotionally, and in social relationships with patients' intimate partners; and (3) barriers to adherence with recommended therapy. Solutions recommended by patients include better education of physicians regarding vulvodynia and the development of multidisciplinary programs that provide access to physiotherapy, sex therapy, mindfulness and psychology services on-site, information classes for new patients, and the creation of peer support networks for patients and their partners. **CONCLUSION:** A patient-focused needs assessment suggests optimal vulvodynia care requires better education of physicians and a multimodal approach to therapy, ideally with multiple services offered in 1 location.

## Provoked Vestibulodynia

### **A review of the available clinical therapies for vulvodynia management and new data implicating proinflammatory mediators in pain elicitation.**

Falsetta ML, Foster DC, Bonham AD, Phipps RP.

*BJOG*. 2016 Jun 17. doi: 10.1111/1471-0528.14157.

<http://www.ncbi.nlm.nih.gov/pubmed/27312009>

Localised provoked vulvodynia (LPV) is a common, chronic, and disabling condition: patients experience profound pain and a diminished quality of life. The aetiologic origins of vulvodynia are poorly understood, yet recent evidence suggests a link to site-specific inflammatory responses. Fibroblasts isolated from the vestibule of LPV patients are sensitive to proinflammatory stimuli and copiously produce pain-associated proinflammatory mediators (IL-6 and PGE<sub>2</sub>). Although LPV is a multifactorial disorder, understanding vulvar inflammation and targeting the inflammatory response should lead to treatment advances, especially for patients exhibiting signs of inflammation. NFκB (already targeted clinically) or other inflammatory components may be suitable therapeutic targets.

### **Differences in Pelvic Morphology Between Women With and Without Provoked Vestibulodynia.**

McLean L, Thibault-Gagnon S, Brooks K, Goldfinger C, Pukall C, Chamberlain S.

*J Sex Med*. 2016 Jun;13(6):963-71. doi: 10.1016/j.jsxm.2016.04.066.

<http://www.ncbi.nlm.nih.gov/pubmed/27215690>

**OBJECTIVE:** Pelvic morphology has been suggested to reflect increased tone and reduced strength of the pelvic floor muscles (PFMs) in women with provoked vestibulodynia (PVD) compared to healthy controls. We aimed to determine whether there are differences in pelvic morphology in the resting state, on maximum voluntary contraction (MVC), or on maximum effort Valsalva maneuver (MVM) between women with and without PVD. **METHODS:** While imaged using ultrasound, 38 women with PVD and 39 controls relaxed their PFMs, performed 3 MVCs and performed 3 MVMs. Levator plate length (LPL), levator plate angle (LPA), and anorectal angle (ARA) were determined at rest, at MVC and at MVM. The displacement of the bladder neck (BN) on MVC and on MVM was also determined. Two-way ANCOVAs were used to evaluate the main effects of group and task, the interaction between group and task, and the effect of resting morphology on LPL, LPA, and ARA. A 2-way repeated-measures ANOVA was used to determine whether the groups differed in terms of BN displacement during the tasks. **RESULTS:** Women with PVD had smaller LPLs and LPAs than controls across all tasks. The significant group differences in LPL and LPA at MVC and MVM were no longer significant once the

resting values were included as covariates in the models. Bladder neck displacement differed between the groups at MVM but not at MVC. **CONCLUSION:** Women with PVD display shorter LPL and smaller LPAs than controls but their behavior does not differ when MVC and MVMs are performed. Our results do not support the hypothesis that women with PVD demonstrate abnormalities in PFM contractility on MVC or compliance on MVM.

**Relationship between nongenital tender point tenderness and intravaginal muscle pain intensity: ratings in women with provoked vestibulodynia and implications for treatment.**

Phillips N, Brown C, Bachmann G, Wan J, Wood R, Ulrich D, Bachour C, Foster D.

*Am J Obstet Gynecol.* 2016 Jul 1. pii: S0002-9378(16)30392-1. doi: 10.1016/j.ajog.2016.06.047.

<http://www.ncbi.nlm.nih.gov/pubmed/27377821>

**BACKGROUND:** Vulvodynia is a chronic vulvar pain disorder and fibromyalgia is a chronic widespread musculoskeletal pain disorder, both of unknown etiology. Association of these conditions is well documented. Intravaginal algometer measurement of tenderness to pressure applied to the pelvic floor muscles helps define vulvodynia associated with musculoskeletal factors. Women with both vulvodynia and fibromyalgia might have increased pelvic muscle pain compared to women with vulvodynia alone, defining the possible link of these 2 conditions. **OBJECTIVE:** We sought to: (1) correlate pain intensity during the nongenital tender point tenderness examination to pain intensity with the vaginal algometer in women with provoked vestibulodynia, and (2) determine whether subjects with provoked vestibulodynia and fibromyalgia had higher pain intensity scores with the vaginal algometer than those without fibromyalgia. **STUDY DESIGN:** In all, 92 subjects referred for vulvar pain were confirmed to have provoked vestibulodynia using the cotton swab test. A diagnosis of fibromyalgia was made if pain was present (numeric rating scale >1) in at least 11 sites of the 18-point nongenital tender point tenderness exam. Vaginal pain sensitivity was measured using an intravaginal pressure algometer, where 0.1, 0.3, and 0.5 kg/cm<sup>2</sup> forces were applied digitally in random assignment by force and location to the right and left iliococcygeus muscle regions and the posterior vaginal wall. Both tender point tenderness and algometer pain intensity were reported on a 0 (no pain) to 10 (worse pain) numeric rating scale. Correlations were computed between the composite pain intensity (total of rating scale from each pressure threshold at specified site) of nongenital and those of iliococcygeus regions and the posterior vaginal wall. Independent t tests were used to determine differences in iliococcygeus regions and the posterior vaginal algometer pain ratings and presence or absence of fibromyalgia. The significance level was at  $P < .05$ . The data were expressed as mean  $\pm$  SD. **RESULTS:** A significant correlation was found between numeric rating scale pain scores on the nongenital tender point tenderness exam and algometer testing on the iliococcygeus region ( $r = 0.44$ ,  $P < .0001$ ) and the posterior vaginal wall ( $r = 0.45$ ,  $P < .0001$ ). Subjects with fibromyalgia by tender point tenderness had significantly higher iliococcygeal pain ( $6.14 \pm 2.07$  vs  $3.74 \pm 2.22$ ,  $P = .0001$ ) and posterior vaginal wall pain ( $5.67 \pm 2.10$  vs  $3.07 \pm 2.16$ ,  $P < .0001$ ) than women without fibromyalgia by tender point tenderness. **CONCLUSION:** Women with provoked vestibulodynia who experience more severe pain with nongenital tender point palpation also experience more deep vaginal pain on pelvic exam. Those who fulfill the diagnosis of fibromyalgia show significantly more intense deep vaginal pain to palpation of iliococcygeus muscles and posterior vaginal wall. Further research using a more precise definition of fibromyalgia is necessary to confirm this relationship, but findings suggest that women with provoked vestibulodynia coexisting with fibromyalgia have greater risk of superimposed vaginal muscle pain and may be candidates for early adjunctive pelvic floor physical therapy. These findings need to be explored in women with generalized, nonprovoked vulvodynia.

## **Immune activation enhances epithelial nerve growth in provoked vestibulodynia.**

Tommola P, Unkila-Kallio L, Paetau A, Meri S, Kalso E, Paavonen J.

*Am J Obstet Gynecol.* 2016 Jul 25. pii: S0002-9378(16)30472-0. doi: 10.1016/j.ajog.2016.07.037.

<http://www.ncbi.nlm.nih.gov/pubmed/27457118>

**BACKGROUND:** Provoked vestibulodynia manifests as allodynia of the vulvar vestibular mucosa. The exact mechanisms that result in altered pain sensation are unknown. Recently, we demonstrated the presence of secondary lymphoid tissue, which is the vestibule-associated lymphoid tissue in the vestibular mucosa, and showed that this tissue becomes activated in provoked vestibulodynia.

**OBJECTIVE:** The purpose of this study was to examine whether expression of intraepithelial nerve fibers and nerve growth factor are related to immune activation in provoked vestibulodynia. **STUDY DESIGN:** Vestibular mucosal specimens were obtained from 27 patients with severe provoked vestibulodynia that was treated by vestibulectomy and from 15 control subjects. We used antibodies against the protein gene product 9.5, the neuron specific neurofilament, and nerve growth factor for immunohistochemistry to detect intraepithelial nerve fibers and nerve growth factor expressing immune cells in the vestibular mucosa. For intraepithelial nerve fibers, we determined their linear density (fiber counts per millimeter of the outer epithelial surface, protein gene product 9.5) or presence (neuron specific neurofilament). Nerve growth factor was analyzed by counting the staining-positive immune cells. Antibodies against CD20 (B lymphocytes) and CD3 (T lymphocytes) were used to identify and locate mucosal areas with increased density of lymphocytes and the presence of germinal centers (ie, signs of immune activation). B-cell activation index was used to describe the overall intensity of B-cell infiltration. **RESULTS:** We found more protein gene product 9.5-positive intraepithelial fibers in vestibulodynia than in the control samples (6.3/mm [range, 0.0-15.8] vs 2.0/mm [range, 0.0-12.0];  $P=.006$ ). Neuron specific neurofilament -positive intraepithelial fibers were found in 17 of 27 vestibulodynia cases (63.0%) and in none of the control cases. Protein gene product 9.5-positive intraepithelial fibers were more common in samples with more pronounced immune activation. The density of these fibers was higher in samples with than without germinal centers (6.1/mm [range, 4.3-15.8] vs 3.0/mm [range, 0.0-13.4];  $P=.020$ ). A positive correlation between the fiber density and B-cell activation index score of the sample was found (Spearman's Rho, 0.400;  $P=.004$ ;  $R^2=0.128$ ). No significant difference, however, was found in the density or presence of nerve fibers between samples with high and low T-cell densities. We identified areas of minor and major vestibular glands in 16 of the patient samples and in 1 control sample. Protein gene product 9.5-positive nerve fibers were found more often in glandular epithelium surrounded by B-cell infiltration than in glands without B cells ( $P=.013$ ). Also, the presence of neuron specific neurofilament-positive fibers in glandular epithelium was associated with B-cell infiltrates ( $P=.053$ ). Nerve growth factor-positive immune cells were more common in mucosal areas with than without B-cell infiltration and intraepithelial nerve fibers. **CONCLUSION:** Excessive epithelial nerve growth in provoked vestibulodynia is associated with increased B-cell infiltration and the presence of germinal centers. This supports the fundamental role of immune activation in provoked vestibulodynia.

## **A review of the available clinical therapies for vulvodynia management and new data implicating proinflammatory mediators in pain elicitation.**

Falsetta ML, Foster DC, Bonham AD, Phipps RP.

*BJOG*. 2016 Jun 17. doi: 10.1111/1471-0528.14157.

<http://www.ncbi.nlm.nih.gov/pubmed/27312009>

Localised provoked vulvodynia (LPV) is a common, chronic, and disabling condition: patients experience profound pain and a diminished quality of life. The aetiologic origins of vulvodynia are poorly understood, yet recent evidence suggests a link to site-specific inflammatory responses. Fibroblasts isolated from the vestibule of LPV patients are sensitive to proinflammatory stimuli and copiously produce pain-associated proinflammatory mediators (IL-6 and PGE<sub>2</sub>). Although LPV is a multifactorial disorder, understanding vulvar inflammation and targeting the inflammatory response should lead to treatment advances, especially for patients exhibiting signs of inflammation. NFκB (already targeted clinically) or other inflammatory components may be suitable therapeutic targets.

## **Local and Systemic Inflammation in Localized, Provoked Vestibulodynia: A Systematic Review.**

Chalmers KJ, Madden VJ, Hutchinson MR, Moseley GL.

*Obstet Gynecol*. 2016 Aug;128(2):337-47. doi: 10.1097/AOG.0000000000001510.

<http://www.ncbi.nlm.nih.gov/pubmed/27400010>

**OBJECTIVE:** To synthesize and critically evaluate all available evidence investigating whether localized, provoked vestibulodynia is associated with a specific inflammatory profile at both a local and a systemic level. **DATA SOURCES:** Comprehensive electronic searches were performed in MEDLINE, EMBASE, Scopus, PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature, the Cochrane Collaboration databases, and ClinicalTrials.gov. The search strategy was developed using MeSH terms related to localized, provoked vestibulodynia, and inflammatory markers. **METHODS OF STUDY SELECTION:** Two independent investigators screened titles and abstracts and performed data extraction and risk of bias assessments. Studies were included if they reported at least one baseline inflammatory marker in women with localized, provoked vestibulodynia and compared them with healthy women. Reference lists from published reviews on localized, provoked vestibulodynia were screened for additional studies. **TABULATION, INTEGRATION, AND RESULTS:** There were 1,619 studies identified. Eighteen studies met the inclusion criteria, including 400 women with localized, provoked vestibulodynia and 212 healthy women in a control group. Risk of bias assessment revealed that the methodologic quality was generally low. Fifteen studies investigated local inflammation and three studies investigated systemic inflammation. On a local level, the number of mast cells expressed in vestibular tissues was greater in women with localized, provoked vestibulodynia expressed than in women in the control group. Several studies reported undefined inflammatory infiltrate in vestibular tissues to a greater level in women with localized, provoked vestibulodynia than in women in the control group. Systemically, levels of natural killer cells were lower in women with localized, provoked vestibulodynia than in women in the control group. There were no systemic differences in systemic interferon-α and interferon-γ levels between groups. **CONCLUSION:** There is limited and contradictory evidence regarding the characteristics of local and systemic inflammation in women with localized, provoked vestibulodynia.

## Physical Therapy

### **Physical Therapy in the Treatment of Central Pain Mechanisms for Female Sexual Pain.**

Vandyken C, Hilton S.

Sex Med Rev. 2016 Aug 3. pii: S2050-0521(16)30025-7. doi: 10.1016/j.sxmr.2016.06.004.

<http://www.ncbi.nlm.nih.gov/pubmed/27498209>

**INTRODUCTION:** The complexity of female sexual pain requires an interdisciplinary approach. Physical therapists trained in pelvic health conditions are well positioned to be active members of an interdisciplinary team addressing the assessment and treatment of female sexual pain. Changes within physical therapy practice in the last ten years have resulted in significant utilization of pelvic floor muscle relaxation and manual therapy techniques to address a variety of pelvic pain conditions, including female sexual pain. However, sexual pain is a complex issue giving credence to the necessity of addressing all of the drivers of the pain experience- biological, psychological and social. **AIM:** This review aims to reconcile current pain science with a plan for integrating a biopsychosocial approach into the evaluation and subsequent treatment for female sexual pain for physical therapists. **METHODS:** A literature review of the important components of skilled physical therapy interventions is presented including the physical examination, pain biology education, cognitive behavioral influences in treatment design, motivational interviewing as an adjunct to empathetic practice, and the integration of non-threatening movement and mindfulness into treatment. **MAIN OUTCOME MEASURE:** A single case study is used to demonstrate the biopsychosocial framework utilized in this approach. **RESULTS:** Appropriate measures for assessing psychosocial factors are readily available and inform a reasoned approach for physical therapy design that addresses both peripheral and central pain mechanisms. Decades of research support the integration of a biopsychosocial approach in the treatment of complex pain, including female sexual pain. **CONCLUSION:** It is reasonable for physical therapists to utilize evidence based strategies such as CBT, pain biology education, Mindfulness Based Stress Reduction (MBSR), yoga and imagery based exercises to address the biopsychosocial components of female sexual pain.

## Dyspareunia

### **The Impact of a Woman's Dyspareunia, and its Treatment, on her Intimate Partner: A Qualitative Analysis.**

Sadownik LA, Smith KB, Hui A, Brotto LA.

J Sex Marital Ther. 2016 Jul 11:0.

<http://www.ncbi.nlm.nih.gov/pubmed/27398766>

This study explored the experiences of male partners of women with dyspareunia, secondary to provoked vestibulodynia (PVD), who participated in the Multidisciplinary Vulvodynia Program (MVP). Participants were 16 men between 22 and 45 years of age. Data was collected with semi-structured interviews and analyzed using content analysis. Men were interviewed about: (1) the impact of the woman's PVD on themselves; and (2) the impact of the MVP on themselves. Participants experienced negative psychological effects (e.g., guilt) in addition to activating emotions (e.g. frustration). They reported diminished quantity and quality of sex. Coping with pain caused relationship strain, communication challenges, and possibilities for relationship growth. The benefits, perceived by the

partner, of the women participating in the treatment program included improvements in knowledge, communication, and psychological and sexual health.

## Co-morbid Disorders

### **Multifactorial contributors to the severity of chronic pelvic pain in women.**

Yosef A, Allaire C, Williams C, Ahmed AG, Al-Hussaini T, Abdellah MS, Wong F, Lisonkova S, Yong PJ. *Am J Obstet Gynecol.* 2016 Jul 18. pii: S0002-9378(16)30457-4. doi: 10.1016/j.ajog.2016.07.023. <http://www.ncbi.nlm.nih.gov/pubmed/27443813>

**BACKGROUND:** Chronic pelvic pain affects ~15% of women, and is associated with significant societal cost and impact on women's health. Identifying factors involved in chronic pelvic pain is challenging due to its multifactorial nature and confounding between potential factors. For example, while some women with endometriosis have chronic pelvic pain, there may be comorbid conditions that are implicated in the chronic pelvic pain rather than the endometriosis itself. **OBJECTIVE:** We sought to explore multifactorial variables independently associated with the severity of chronic pelvic pain in women. **STUDY DESIGN:** We used baseline cross-sectional data from an ongoing prospective cohort, collected from patient online questionnaires, physical examination, and physician review of medical records. Participants were recruited from a tertiary referral center for endometriosis and chronic pelvic pain in Vancouver, British Columbia, Canada, from December 2013 through April 2015. Exclusion criteria included menopausal status or age >50 years. Primary outcome was self-reported severity of chronic pelvic pain in the last 3 months (0-10 numeric rating scale). Potential associated factors ranged from known pain conditions assessed by standard diagnostic criteria, validated psychological questionnaires, musculoskeletal physical exam findings, as well as pain-related, reproductive, medical/surgical, familial, demographic, and behavioral characteristics. Mann-Whitney, Kruskal-Wallis, or Spearman test were used to identify variables with an association with the primary outcome ( $P < .05$ ), followed by multivariable linear regression to control for confounding and to identify independent associations with the primary outcome ( $P < .05$ ). **RESULTS:** Overall, 656 women were included (87% consent rate), of whom 55% were diagnosed with endometriosis. The following factors were independently associated with higher severity of chronic pelvic pain: abdominal wall pain ( $P = .005$ ), pelvic floor tenderness ( $P = .004$ ), painful bladder syndrome ( $P = .019$ ), higher score on Pain Catastrophizing Scale ( $P < .001$ ), adult sexual assault ( $P = .043$ ), higher body mass index ( $P = .023$ ), current smoking ( $P = .049$ ), and family history of chronic pain ( $P = .038$ ). Severity of chronic pelvic pain was similar between women with and without endometriosis. **CONCLUSION:** Multifactorial variables independently associated with severity of chronic pelvic pain were identified, ranging from myofascial/musculoskeletal, urological, family history, and psycho-social factors. Continued research is required to validate these factors and to determine whether any are potentially modifiable for the management of chronic pelvic pain.

## **Persistent Genital Arousal Disorder: A Review of Its Conceptualizations, Potential Origins, Impact, and Treatment.**

Jackowich RA, Pink L, Gordon A, Pukall CF.

*Sex Med Rev.* 2016 Jul 22. pii: S2050-0521(16)30024-5. doi: 10.1016/j.sxmr.2016.06.003.

<http://www.ncbi.nlm.nih.gov/pubmed/27461894>

**INTRODUCTION:** Persistent genital arousal disorder (PGAD) is a condition characterized by symptoms of physiologic (typically genital) sexual arousal in the absence of perceived subjective sexual arousal. The physiologic arousal can last hours or days, or it can occur constantly, and it does not typically remit after orgasm(s). The symptoms are usually described as distressing, intrusive, and unwanted. **AIM:** To review the available literature on PGAD. **METHODS:** A literature review through April 2016 was undertaken using terms persistent genital arousal disorder, persistent sexual arousal syndrome, and restless genital syndrome. **MAIN OUTCOME MEASURES:** The main outcome is a review of the conceptualization of PGAD, its prevalence, proposed etiologies and treatments, and its impact on psychosocial and sexual functioning. **RESULTS:** Much of the research on the potential etiologies and treatments of PGAD is published in the form of case studies. Several etiologies of PGAD have been proposed; however, a cause or causes have not been confirmed. A range of treatments has been explored primarily in case studies, from electroconvulsive therapy to oral medication, with variable success rates. Psychologically based treatments have been suggested but have yet to be evaluated. Online surveys have found initial evidence supporting the negative impact of PGAD on mental health and sexual functioning; however, more research is needed in this area. **CONCLUSION:** Although PGAD was first conceptualized 15 years ago, it remains a very under-researched condition. Currently, little is known about its biopsychosocial correlates, etiologies, or successful treatments. Future research directions are identified.

## **Combined site-specific sacral neuromodulation and pudendal nerve release surgery in a patient with interstitial cystitis and persistent arousal.**

Armstrong GL, Vancaillie TG.

*BMJ Case Rep.* 2016 Jun 9;2016. pii: bcr2015213513. doi: 10.1136/bcr-2015-213513.

<http://www.ncbi.nlm.nih.gov/pubmed/27284095>

A variety of neuromodulation approaches have been described for the management of pelvic neuropathies, including interstitial cystitis, pudendal neuralgia and persistent genital arousal disorder. The benefits of a combined sacral and pudendal nerve neuromodulator has yet to be explored for these patients. In this report, we describe the case of a 35-year-old woman with a complex pelvic neuropathy resulting in urinary, sexual and gastro-intestinal dysfunction. She presented with an established diagnosis of interstitial cystitis; however, she also fulfilled diagnostic criteria for pudendal neuralgia and persistent genital arousal disorder. The patient underwent implantation of a combined sacral and pudendal nerve neuromodulation device at the time of surgical decompression of the pudendal nerves. An impressive clinical response followed. This case demonstrates a unique clinical presentation and highlights the value of a combined surgical and neuromodulatory approach in the management of patients with complex pelvic neuropathies.

### **Adding corticosteroids to the pudendal nerve block for pudendal neuralgia: a randomised, double-blind, controlled trial.**

Labat JJ, Riant T, Lassaux A, Rioult B, Rabischong B, Khalfallah M, Volteau C, Leroi AM, Ploteau S. *BJOG*. 2016 Jul 27. doi: 10.1111/1471-0528.14222. <http://www.ncbi.nlm.nih.gov/pubmed/27465823>

**OBJECTIVE:** To compare the effect of corticosteroids combined with local anaesthetic versus local anaesthetic alone during infiltrations of the pudendal nerve for pudendal nerve entrapment. **DESIGN:** Randomised, double-blind, controlled trial. **SETTING:** Multicentre study. **POPULATION:** 201 patients were included in the study, with a subgroup of 122 women. **METHODS:** CT-guided pudendal nerve infiltrations were performed in the sacrospinous ligament and Alcock's canal. There were three study arms: patients in Arm A (n = 68) had local anaesthetic alone, those in Arm B (n = 66) had local anaesthetic plus corticosteroid and those in Arm C (n = 67) local anaesthetic plus corticosteroid with a large volume of normal saline. **MAIN OUTCOME MEASURES:** The primary end-point was the pain intensity score at 3 months. Patients were regarded as responders (at least a 30-point improvement on a 100-point visual analogue scale of mean maximum pain over a 2-week period) or nonresponders. **RESULTS:** Three months' postinfiltration, 11.8% of patients in the local anaesthetic only arm (Arm A) were responders versus 14.3% in the local anaesthetic plus corticosteroid arms (Arms B and C). This difference was not statistically significant (P = 0.62). No statistically significant difference was observed in the female subgroup between Arm A and Arms B and C (P = 0.09). No significant difference was detected for the various pain assessment procedures, functional criteria or quality-of-life criteria. **CONCLUSIONS:** Corticosteroids provide no additional therapeutic benefits compared with local anaesthetic and should therefore no longer be used. **TWEETABLE ABSTRACT:** Steroid infiltrations do not improve the results of local anaesthetic infiltrations in pudendal neuralgia.

### **Pudendal neuralgia after pelvic surgery using mesh: Case reports and laparoscopic pudendal nerve decompression.**

Sancak EB, Avci E, Erdogru T. *Int J Urol*. 2016 Jun 2. doi: 10.1111/iju.13136. <http://www.ncbi.nlm.nih.gov/pubmed/27250921>

Persistent pain after vaginal mesh surgery is a rare and agonizing entity that has devastating consequences for the patient's quality of life. Many etiologies have been blamed including nerve injuries and entrapments. Pudendal neuralgia is a rare chronic neuropathic pain syndrome in the anatomical territory of the pudendal nerve. Various treatment options, such as medication management, physiotherapy, nerve blocks, decompression surgery and neuromodulation, have been used, but the most appropriate treatment for pudendal neuralgia has not yet been determined. In this article, we present two cases of postoperative pelvic pain thought to be secondary to injury or mechanical distortion of the pudendal nerve after rectocele repair using mesh and tension-free vaginal tape sling. In cases of failed conservative treatment and of mesh removal surgery, laparoscopic pudendal nerve decompression and omental flap wrapping operation can be a treatment option for pudendal neuralgia.

### **A Qualitative Study on Experiences After Vulvar Surgery in Women With Lichen Sclerosis and Sexual Pain.**

Brauer M, van Lunsen RH, Laan ET, Burger MP.

*J Sex Med.* 2016 Jul;13(7):1080-90. doi: 10.1016/j.jsxm.2016.04.072. Epub 2016 May 18.

<http://www.ncbi.nlm.nih.gov/pubmed/27209180>

**INTRODUCTION:** Lichen sclerosis (LS) of the vulva can profoundly affect sexual interaction because of painful fissures and narrowing of the vaginal introitus. Successful surgical treatment is usually defined as restoration of (pain-free) penetrative sexual activity. **AIMS:** To evaluate the impact of surgery on (dyadic) sexual functioning and pleasure and psychological well-being. **METHODS:** Nineteen women with anogenital LS participated in audiotaped, qualitative, individual interviews after surgery to re-enable sexual intercourse. **MAIN OUTCOME MEASURES:** Physical, sexual, and psychological experiences were analyzed using the constant comparative method. **RESULTS:** Vulvar surgery resulted in a decrease of sexual pain in 13 of 19 patients (68%). Of these 13 patients, 4 were completely free of pain and the other 9 patients expressed a shift from preoperative sexual pain to postoperative sexual discomfort. These women reported improved sexual functioning, increased sexual activity and intimacy with the partner, and reinstated feelings of being an adequate woman and sexual partner. In 1 of the 19 patients (5%), surgery did not result in decreased sexual pain, yet she continued to have intercourse. Five of the 19 patients (26%) stopped having intercourse because of pain; one woman had secondary vaginismus and another woman, in retrospect, had premorbid generalized unprovoked vulvodynia. Four of these women were unable to communicate with their partner about sexual matters and to change their sexual repertoire (satisfactorily) once they had ceased intercourse (attempts). Eighteen women (95%) reported a decrease of LS symptoms in daily life. **CONCLUSION:** Vulvar surgery seems an effective treatment for most women with LS who experience sexual pain owing to anatomic or epithelial changes and who wish to resume intercourse. To assess whether women might benefit from such surgery and/or whether (additional) sexual counseling is indicated, preoperative sexological couple-based consultation is needed. This consultation should exclude comorbid vaginismus and generalized unprovoked vulvodynia and index the couple's pre-existing sex life, including sexual communication skills, and the ability to incorporate non-coital pain-free sexual activities.

### **Comparison of 5-Aminolevulinic Acid Photodynamic Therapy and Clobetasol Propionate in Treatment of Vulvar Lichen Sclerosis.**

Shi L, Miao F, Zhang LL, Zhang GL, Wang PR, Ji J, Wang XJ, Huang Z, Wang HW, Wang XL.

*Acta Derm Venereol.* 2016 Jun 15;96(5):684-8. doi: 10.2340/00015555-2341.

<http://www.ncbi.nlm.nih.gov/pubmed/26775671>

The aim of this study was to evaluate the effectiveness of 5-aminolevulinic acid photodynamic therapy (ALA-PDT) for the treatment of vulvar lichen sclerosis (VLS) and compare its effectiveness with that of clobetasol propionate. Four sessions of topical photodynamic therapy (PDT) were administered at 2-week intervals ( $n = 20$ ). Clobetasol propionate (0.05%) was used daily for 8 weeks ( $n = 20$ ). The rate of complete response in the PDT group (14/20) was double that of the clobetasol propionate group (7/20) ( $p < 0.05$ ,  $2 = 4.912$ ). Horizontal visual analogue scores indicated that PDT was more effective than clobetasol propionate. Pain intensity numeric rating scale values for PDT were between 3.05 and 4.45.

One month after the final session of PDT, only one patient relapsed and all 7 patients in clobetasol propionate group relapsed. ALA-PDT is a well-tolerated and effective option for the treatment of VLS.

### **New insights into potential risk factors and associations in genital lichen sclerosus: Data from a multicentre Italian study on 729 consecutive cases.**

Virgili A, Borghi A, Cazzaniga S, Di Landro A, Naldi L, Minghetti S, Verrone A, Stroppiana E, Caproni M, Nasca MR, D'Antuono A, Papini M, Di Lernia V, Corazza M; GLS Italian Study Group.

*J Eur Acad Dermatol Venereol.* 2016 Aug 12. doi: 10.1111/jdv.13867.

<http://www.ncbi.nlm.nih.gov/pubmed/27515901>

**BACKGROUND:** Limited data are available on risk factors associated with lichen sclerosus and no data are available on gender differences in genital lichen sclerosus (GLS). **OBJECTIVE:** This multicentre study aimed at identifying potential risk factors for GLS, through data collection from a large, mixed-sex sample of patients comparing gender-related differences in relation to data from the general population. **METHODS:** This was a cross-sectional study on 729 subjects (53.8% females, 46.2% males) affected with GLS, consecutively observed within a network of 15 Italian dermatology units. The following information was collected: demographic data, anthropometric measures, comorbidities, family history of LS, clinical features and symptoms related to GLS. **RESULTS:** Overweight and obesity, blood hypertension, hypothyroidism and an educational attainment equal or above upper secondary school level were more frequent among the study patients than among the general Italian population. Moreover, a family history of GLS was reported more frequently than expected among GLS patients. These factors were similar in males and females. The disease tended to occur later in females than in males. **CONCLUSIONS:** Our findings suggest that metabolic factors, and possibly a sedentary lifestyle, may play a role in GLS pathogenesis in genetically predisposed patients, and that risk profile is similar in males and females despite some difference in the onset of symptoms.

### **Effects of Intravenous Ketamine Infusions in a Neuropathic Pain Patient with Lichen Sclerosus et Atrophicus.**

Hanna AF, Armstrong JS, Smith AJ.

*Case Rep Dermatol.* 2016 Jun 6;8(2):164-70. doi: 10.1159/000446528.

<http://www.ncbi.nlm.nih.gov/pubmed/27462225>

A patient reported to the Florida Spine Institute (Clearwater, Fla., USA) with severe lichen sclerosus of the anogenital region and legs. The patient's pain presentation was neuropathic with hypersensitivity, allodynia, swelling, and weakness. The patient had failed multiple pain management modalities including opioid therapy, anticonvulsants, and antidepressants. The patient completed a standard intravenous ketamine infusion regimen developed at the Florida Spine Institute and reported complete abolishment of her pain syndrome. For the first time, we report that ketamine infusions also dramatically improved a patient's lichen sclerosus. That ketamine is known to have immunomodulatory properties, and given the clinical observations described in this case report, suggests that ketamine should be explored as a possible new therapeutic option for managing lichen sclerosus, especially in cases that are refractory to conventional therapies.

### **Common prepubertal vulvar conditions.**

Vilano SE, Robbins CL.

Curr Opin Obstet Gynecol. 2016 Aug 11

<http://www.ncbi.nlm.nih.gov/pubmed/27517340>

**PURPOSE OF REVIEW:** The purpose of this article is to provide an update for the GP on selected common vulvar concerns in prepubertal girls. Presentation, diagnostic criteria, and management of common vulvar conditions will be described. The following conditions are frequently encountered and may pose diagnostic or management challenges if unrecognized. **RECENT FINDINGS:** The article is a review of current literature on pediatric vulvar conditions and was conducted through searching PubMed and published books on this topic. Areas of interest frequently encountered by providers are presented, including vulvovaginitis, genital ulcers, lichen sclerosus, and labial adhesions along with the most recent North American Society for Pediatric and Adolescent Gynecology recommendations for diagnosis and management. **SUMMARY:** Vulvar complaints in prepubertal girls are common. Many present with nonspecific symptoms and consequently, the diagnosis may be missed or delayed. Prompt recognition improves long-term outcomes and importantly, provides a positive introduction to longitudinal women's health for young girls.