

Research Update E- Newsletter

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## Vulvodynia

### **Changes in the Vaginal Microbiota of Women With Secondary Localized Provoked Vulvodynia**

Yaseen Awad-Igbaria, Eilam Palzur, Manal Nasser, Pedro Vieira-Baptista, Jacob Bornstein

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**Objective:** The etiology of localized provoked vulvodynia (LPV) remains unknown, but observations suggest the involvement of the vaginal microbiota. We examined the vaginal microbiota of women with LPV and healthy controls, upon after a low-oxalate diet (LOD). **Materials and methods:** A total of 9 women diagnosed with secondary LPV and 21 healthy controls were recruited from the Galilee Medical Center in Israel and subjected to prospective evaluations of their vaginal microbiota. Total DNA was extracted from vaginal discharge samples provided before and after following LOD for 3 weeks and was then subjected to 16S sequencing. Data obtained were then used to evaluate  $\alpha$  and  $\beta$  diversity, identify differentially abundant bacterial taxa in LPV, and determine their impact on the metabolism.

**Results:** These evaluations revealed decreased diversity in the vaginal microbiota of women with LPV and identified the Ochrobactrum genus and Pseudomonadaceae family as indicators for LPV. In addition, we identified 23 differentially expressed bacterial metabolic pathways between the LPV and control samples and revealed that LOD could induce changes in the  $\beta$  diversity of LPV vaginal microbiomes, which was further supported by some degree of pain reduction in patients. **Conclusions:** Localized provoked vulvodynia and LOD were associated with shifts in the vaginal microbiota. However, the impact of these changes on the development of LPV requires additional studies with a larger cohort.

### **Symptom-associated alterations in functional connectivity in primary and secondary provoked vestibulodynia**

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Primary provoked vestibulodynia (PVD) is marked by onset of symptoms at first provoking vulvar contact, while secondary PVD refers to symptom onset after some period of painless vulvar contact.

Different pathophysiological processes are thought to be involved in the development and maintenance of primary PVD and secondary PVD. The primary aim of this study was to test the hypotheses that the resting state functional connectivity of the brain and brainstem regions differs between these subtypes. Deep clinical phenotyping and resting state brain imaging were obtained in a large sample of a women with primary PVD (n=46), secondary PVD (n=68) and healthy controls (n=94). The general linear model was used to test for differences in region-to-region resting state functional connectivity and psychosocial and symptom assessments. Direct statistical comparisons by onset type indicated that women with secondary PVD have increased dorsal attention-somatomotor network connectivity whereas women with primary PVD predominantly show increased intrinsic resting state connectivity within the brainstem and the default mode network. Furthermore, women with secondary PVD compared to primary PVD reported greater incidence of early life sexual abuse, greater pain catastrophizing, greater 24-hour symptom unpleasantness and less sexual satisfaction. The findings suggest that women with secondary PVD show greater evidence for central amplification of sensory signals whereas women with primary PVD have alterations in brainstem circuitry responsible for the processing and modulation of ascending and descending peripheral signals.

### **Provoked Vestibulodynia and Topical Treatment: A New Option**

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Healthcare (Basel). 2022 Apr 30;10(5):830. doi: 10.3390/healthcare10050830.  
<https://pubmed.ncbi.nlm.nih.gov/35627968/>

**Background:** Provoked vestibulodynia is commonly associated with dyspareunia and affects 7% to 15% of women. This pathology has major implications on sexual function and quality of life, and several types of treatments are available for its management. However, a consensus has not been reached concerning the best treatment of vulvar pain. The aim of this study was to assess the efficacy and safety of a brand-new product, the vulvar emulgel Meclon<sup>®</sup> Lenex, for the management of provoked vestibulodynia and non-infective vulvitis. **Methods:** This was a monocentric, prospective, randomized, double-blind and placebo-controlled study. We enrolled 40 women with provoked vestibulodynia; 20 patients received Meclon<sup>®</sup> Lenex, whereas the remaining received a placebo. Each woman was assessed subjectively (through questionnaires) and objectively by evaluating vaginal and vulvar symptoms (Friedrichs criteria and Marinoff dyspareunia grade). We evaluated efficacy, safety, compliance and tolerability of the brand-new product vulvar gel Meclon<sup>®</sup> Lenex in provoked vestibulodynia. **Results:** After administration of Meclon<sup>®</sup> Lenex, we evaluated all parameters of the Friedrichs criteria (burning, dyspareunia, erythema, vulvar pain at the 5 o'clock position and 7 o'clock position), as well as the levels of Marinoff dyspareunia. The active treatment showed to be statistically significantly effective ( $p$  value  $\leq 0.05$ ) in reducing all symptoms of Friedrichs criteria, vulvar pain and Marinoff dyspareunia. **Conclusion:** This prospective study showed that Meclon<sup>®</sup> Lenex vulvar emulgel revealed an excellent tolerability and compliance, demonstrating to be a safe and effective option in the treatment of provoked vestibulodynia and non-infective vulvitis.

### **Characterization of Early Inflammatory Events Leading to Provoked Vulvodynia Development in Rats**

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<https://pubmed.ncbi.nlm.nih.gov/35845089/>

**Background:** Provoked vulvodynia (PV) is the main cause of vulvar pain and dyspareunia. The etiology of PV has not yet been elucidated. However, PV is associated with a history of recurrent inflammation, and its often accompanied by increases in the numbers of mast cells (MCs) and sensory hyperinnervation in the vulva. Therefore, this study aimed to examine the role of MCs and the early inflammatory events in the development of chronic vulvar pain in a rat model of PV. **Methods:** Mechanical and thermal vulvar sensitivity was measured for 5 months following zymosan vulvar challenges. Vulvar changes in glutamate and nerve growth factor (NGF) were analyzed using ELISA. Immunofluorescence (IF) staining of the vulvar section after 20, 81, and 160 days of the zymosan challenge were performed to test MCs accumulation, hyperinnervation, and expression of pain channels (transient receptor potential vanilloid/ankyrin-1-TRPV1 & TRPA1) in vulvar neurons. Changes in the development of vulvar pain were evaluated following the administration of the MCs stabilizer ketotifen fumarate (KF) during zymosan vulvar challenges. **Results:** Zymosan-challenged rats developed significant mechanical and thermal vulvar sensitivity that persisted for over 160 days after the zymosan challenge. During inflammation, increased local concentrations of NGF and glutamate and a robust increase in MCs degranulation were observed in zymosan-challenged rats. In addition, zymosan-challenged rats displayed sensory hyperinnervation and an increase in the expression of TRPV1 and TRPA1. Treatment with KF attenuated the upregulated level of NGF during inflammation, modulated the neuronal modifications, reduced MCs accumulation, and enhanced mechanical hypersensitivity after repeated inflammation challenges. **Conclusion:** The present findings suggest that vulvar hypersensitivity is mediated by MCs accumulation, nerve growth, and neuromodulation of TRPV1 and TRPA1. Hence, KF treatment during the critical period of inflammation contributes to preventing chronic vulvar pain development.

### **High-Intensity Laser Therapy (HILT) as an Emerging Treatment for Vulvodynia and Chronic Musculoskeletal Pain Disorders: A Systematic Review of Treatment Efficacy**

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High-intensity laser therapy (HILT) has been gaining popularity in the treatment of chronic musculoskeletal pain, including vulvodynia. The objective of this study was to critically appraise and synthesize the available evidence on the efficacy of HILT for reducing pain and improving function in vulvodynia and other chronic primary musculoskeletal pain conditions. Electronic databases and the grey literature were searched. Effects on pain intensity, function, and adverse events were assessed. One study investigating HILT in the treatment of vulvodynia and 13 studies on the treatment of chronic musculoskeletal pain were selected. The study assessing vulvodynia showed favorable results for reducing pain. Regarding chronic musculoskeletal pain, 12 out of the 13 studies selected consistently showed that HILT was more effective than the placebo/active comparator for reducing pain and improving function. The available effect sizes for pain showed large to huge effects. Similar effects were observed for function except for two studies showing moderate effects. The GRADE score was moderate. Conclusions: There are insufficient data to support the use of HILT in vulvodynia, but the promising results encourage further research. HILT appears to be effective in musculoskeletal pain conditions. More high-quality studies are needed to identify effective laser protocols.

### **Obstetric outcomes in women with vulvodynia or vaginismus**

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**Purpose:** Vulvodynia and vaginismus are common chronic vulvar pain disorders for which there is a paucity of literature on pregnancy outcomes of affected women. The study objective was to evaluate the associations between vulvodynia and vaginismus and obstetric outcomes. **Methods:** We performed a retrospective cohort study including all birth-related admissions from 1999 to October 2015 extracted from the Healthcare Cost and Utilization Project-National Inpatient Sample from the United States. Women with vulvodynia or vaginismus were identified using the appropriate ICD-9 codes. Multivariate logistic regression models, adjusted for baseline maternal characteristics, were performed to evaluate the effect of vulvodynia and vaginismus on obstetrical and neonatal outcomes. **Results:** A total of 879 obstetrical patients with vulvodynia or vaginismus were identified in our cohort of 13,792,544 patients admitted for delivery in US hospitals between 1999 and 2015, leading to an overall prevalence of 6 cases per 100,000 births. Between 1999 and 2015, the annual prevalence of vulvodynia or vaginismus rose from 2 to 16 cases per 100,000. Vulvodynia and vaginismus were associated with increased risks of eclampsia, chorioamnionitis, post-term pregnancy, cesarean delivery, instrumental vaginal delivery, blood transfusions, prolonged hospital stays, congenital anomalies and intrauterine growth restriction. **Conclusion:** Vulvodynia and vaginismus in pregnancy appears underreported in pregnancy compared to reported population rates. Prevalence of reporting seems to have increased in the last decades and is associated with increased risks of maternal and newborn morbidities. Obstetrical caregivers should be aware of the underreporting of these conditions and the associated adverse effects when counseling obstetrical patients.

### **Vulvodynia: What is available online? A systematic review of information on the internet**

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J Obstet Gynaecol Res. 2022 Aug;48(8):2112-2121. doi: 10.1111/jog.15324. Epub 2022 Jun 14.

<https://pubmed.ncbi.nlm.nih.gov/35699223/>

**Aim:** This review aimed to evaluate the quality of medical information online for patients relating to vulvodynia. To our knowledge no evaluation of online patient information exists regarding vulvodynia and, at present, there is no standardized or validated method of evaluating medical information on the internet. **Methods:** A clearly defined protocol was developed to generate keywords relating to vulvodynia. The three most popular search engines worldwide; google.com, yahoo.com, and bing.com, were searched in September 2020. Three assessors evaluated eligible webpages for accuracy, credibility, readability, and reliability. **Results:** Forty-five webpages were eligible with 38% given HON certification or Information Standard approval. Only one webpage achieved a DISCERN score of  $\geq 63$  indicating excellent reliability. No webpages scored a maximum 10 points for credibility. Eleven percent of webpages were rated "accurate" with score 17 or above. The modal Flesch Kincaid Grade Level was 9 with only 15.6% having a readability grade level of 8 or less. **Conclusions:** It has been shown in previous studies that patient information available online pertaining to gynecological conditions is frequently inaccurate, with limited regulation and low reliability, and our findings are in agreement with this. As patients increasingly look to the internet for medical information and education, we as clinicians, need to ensure the resources available are of a high standard and regulated. Without ensuring safe and effective healthcare resources, we risk misinformation which can negatively impact clinical care.

### **Experiences of internet-based treatment for vulvodynia: A qualitative study**

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<https://pubmed.ncbi.nlm.nih.gov/35870352/>

**Objective:** The aim of this study was to describe women's experiences before, under, and after a guided internet-based intervention for vulvodynia. **Methods:** The design was qualitative, based on content analysis. Participants were women who had undergone guided internet-based treatment for vulvodynia based on acceptance and commitment therapy principles (n = 13). Data were collected through in-depth interviews approximately one month after participants completed treatment. **Results:** The analysis revealed the women's experiences of internet-based treatment for vulvodynia. Three themes emerged: "dealing with pain alone," which was related to experiences of living with vulvodynia before internet-based treatment; "finding new ways," which described the experiences of undergoing an internet-based treatment for vulvodynia and "feeling empowered to take control," referring to the experiences of living with vulvodynia after the internet-based treatment. The women described a long search for a diagnosis, revealing a negative experience of healthcare. The internet-based treatment helped them find new ways to manage vulvodynia, but difficulties with the treatment were also experienced. After the intervention, the women reported improvements in wellbeing and having better strategies to manage pain, but also stated that the treatment was insufficient to perceive changes in vulvar pain. **Conclusions:** The guided internet-based treatment program for vulvodynia based on acceptance and commitment therapy principles was perceived as credible, helpful to manage vulvodynia, and could serve as a complement to regular care. Questions regarding the need for more support and optimal length of treatment need to be further evaluated.

### **Vestibulodynia and the Vaginal Microbiome: A Case-Control Study**

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**Background:** Recent studies of the vaginal microbiome have led to a better understanding of the microbiota and interactions with the host environment, however the role of the vaginal microbiome in vestibulodynia remains unclear. **Aim:** This study aims to investigate and examine differences in the bacterial and fungal microbiome among patients with vestibulodynia and healthy controls. **Methods:** A case-control study was conducted examining the vaginal microbiome of 29 patients with vestibulodynia and 26 controls through Stony Brook University Obstetrics and Gynecology ambulatory clinic. Exclusion criteria included a diagnosis of vaginal infection at the time of presentation, a prior diagnosis of vulvodynia or receipt of treatment, immunosuppression, and receipt of steroid or antibiotic therapy. Vaginal swab samples were obtained from participants. DNA was extracted and sent for diversity assay of 16S rRNA for prokaryotic species and internal transcribed spacers (ITS) for fungi. Demographic characteristics for both cases and controls were obtained through a retrospective chart review. **Outcome measure:** Principal component analysis (PCA) and linear discriminant analysis effect size (LefSe) were used to identify differences in relative abundance of operational taxonomic units (OTUs) for the vaginal microbiome between vestibulodynia patients and controls. **Results:** Lactobacillus species were dominant amongst both cases and controls. PCA of 16S and ITS OTUs did not show significant differences in microbiome composition between vestibulodynia patients and controls. LefSe demonstrated higher abundance of Bifidobacterium longum, the Genus Sneathia, and the Family

Leptotrichiaceae, in controls compared to vestibulodynia samples. For ITS, *Aspergillus* spp. was significantly more prevalent in controls than in vestibulodynia cases. **Clinical implications:** Additional studies are needed to further assess the clinical significance of these findings. **Strengths and limitations:** Strengths of this study include ITS amplicon sequence analysis for fungal species diversity. Limitations of this study include small sample size and lack of racial diversity. **Conclusions:** Our study did not find significant differences in composition or diversity between the vaginal microbiomes of cases of vestibulodynia and controls; however, the data suggests differences in abundance of biota requiring further research for biological and clinical significance.

### **Impact of a single-session psychosocial counseling intervention for women with vulvodynia**

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<https://pubmed.ncbi.nlm.nih.gov/35766991/>

**Objective:** To evaluate the impact of a single session of psychosocial counseling on patients with vulvodynia. **Methods:** Patients diagnosed with vulvodynia at a vulvovaginal specialty clinic were randomly assigned to receive either a one-on-one 30- to 45-min psychosocial counseling session with a psychosexual counselor plus written educational materials (intervention group) or written materials alone (control group). They completed a survey before and 6 weeks after randomization that included demographic information and validated measures of sexual function and illness perception.

**Results:** Thirty-one of 38 (81.6%) women approached chose to participate; 26 of the 31 (83.9%) completed the 6-week follow-up survey. Only the intervention group showed improvement in knowledge about vulvovaginal and sexual health, as well as in most measures of improvement in illness perception, as measured by the Brief Illness Perception Questionnaire ( $P < 0.05$ ). When compared directly with those in the control group, patients in the intervention group reported increased understanding of their vulvar symptoms ( $P < 0.005$ ) and lessened emotional impact of these symptoms ( $P = 0.035$ ). **Conclusion:** Patients receiving one session of the one-on-one psychosocial counseling intervention reported improved understanding and lessened emotional impact of their vulvar symptoms, compared with the control group. This study suggests that improvement may occur following minimal intervention and supports the need for further study.

### **An initial proof of concept: A replicated single-case study of a CBT group treatment with partner involvement for vulvodynia**

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<https://pubmed.ncbi.nlm.nih.gov/35960277/>

Vulvodynia is common and has an immense impact on affected women and their partners. Psychological factors have been found to contribute to pain maintenance and exacerbation, and treatments addressing psychological factors have yielded positive results. This study employed a replicated single-case experimental design to examine a cognitive behavioral therapy (CBT) group treatment with partner involvement in vulvodynia. Repeated measures of pain intensity related to pain-inflicting behaviors were collected weekly throughout baseline and treatment phases. Associated outcomes were measured pre-, post- and at two follow-up assessments. Participants were 18-45-year-old women, in a stable sexual relationship with a man, experiencing vulvodynia. Five women completed the treatment consisting of 10

group sessions and 3 couple sessions. Data were analyzed through visual inspection and supplementary nonparametric calculations. The study showed promising results of the CBT treatment in alleviating pain intensity in connection to specific pain-inflicting behavior since three out of five participants showed improvements. For the participants who improved, sexual function, pain catastrophizing, avoidance, and endurance behavior changed during treatment and were maintained at follow-ups. These results warrant further study of the CBT treatment, in larger, and controlled formats.

### **A conceptual model for managing sexual pain with somatocognitive therapy in women with provoked vestibulodynia and implications for physiotherapy practice**

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Physiother Theory Pract. 2022 Jul 10;1-14. doi: 10.1080/09593985.2022.2096516.

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Somatocognitive therapy is a multimodal physiotherapy treatment developed in the early 2000s to alleviate the burden of chronic pelvic pain. In recent years, somatocognitive therapy has been further developed to treat women with provoked vestibulodynia. This prevalent gynecological pain condition is a subgroup of chronic pelvic pain and the most common form of vulvodynia. Provoked vestibulodynia is a neglected multifactorial pain condition of unknown cause, adversely affecting women's sexual life, relation to their partners and their psychological health. Pain is located at the vulvar vestibule and is provoked by touch or pressure such as sexual intercourse. In the management of sexual pain, somatocognitive therapy combines bodily exploration, pain education, cognitive coping strategies and structured homework to improve sexual function and reduce pain. To support these processes, developing a sound therapeutic alliance with the patient is essential. The aim of this article is to provide a conceptual model for managing provoked vestibulodynia with somatocognitive therapy, including a theoretical rationale for this treatment. We base our conceptual model on the biopsychosocial model, i.e., considering the complex interplay of biomedical, emotional/cognitive, psychosexual and interpersonal factors in provoked vestibulodynia management. In addition, implications for practice and a detailed description of somatocognitive therapy for provoked vestibulodynia will be provided, to allow replication in clinical practice and in clinical trials.

### **Behavioral sex therapy and medications associated in the treatment of provoked vulvodynia: efficacy on pain and sexuality in three illustrative cases**

Anna Ghizzani, Giulia Toto, Stefano Luisi

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This paper tests the hypothesis that medications combined with behavioral sex therapy might lessen pain and restore sexuality in women with provoked vulvodynia. Three women affected by vulvodynia, otherwise healthy, in heterosexual relationship were treated at the Department of Obstetrics and Gynecology in a university hospital. In consecutive sessions of behavioral sex therapy, oral tricyclic antidepressants and vulvar applications of estrogen and hydrocortisone creams were prescribed in association with vaginal dilators and sensate focus exercises. The outcome supports the hypothesis that combined medications and sexual behavior interventions may be effective in lessening pain and restoring sexuality in women with provoked vulvodynia. The different dyadic balances observed in this small case series suggest how to best use this protocol. The positive results appear to be mostly due to

behavioral sex therapy that was the new element added to the combination of pharmacological agents commonly used to treat provoked vulvodynia.

## Chronic Pelvic Pain

### **Female Sexual Dysfunctions and Urogynecological Complaints: A Narrative Review**

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Medicina (Kaunas). 2022 Jul 23;58(8):981. doi: 10.3390/medicina58080981.

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Female sexual dysfunctions represent a real widespread problem, usually faced from a psychological point of view; however, millions of women worldwide are impacted by pelvic floor dysfunction, personal shame and social taboos, however, continue to inhibit free conversation on the subject. Women's quality of life is considerably improved by screening, diagnosing, and controlling urogenital and sexual issues. This review aims to provide a critical perspective of urogenital conditions and common disturbances in female sexual function associated with these issues. It also includes a discussion of postpartum pelvic dysfunction.

### **Chronic Pelvic Pain Profiles in Women Seeking Care in a Tertiary Pelvic Pain Clinic**

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<https://pubmed.ncbi.nlm.nih.gov/35972368/>

**Objective:** Female chronic pelvic pain (CPP) has multiple pain generators and significant psychosocial sequelae. Biopsychosocial-based phenotyping could help identify clinical heterogeneity that may inform tailored patient treatment. This study sought to identify distinct CPP profiles based on routinely collected clinical information and evaluate the validity of the profiles through associations with social histories and subsequent health care utilization. **Methods:** Women (18-77 years, n = 200) seeking care for CPP in a tertiary gynecological pelvic pain clinic between 2017-2020 were included. Baseline data of pain intensity, interference, catastrophizing, acceptance, overlapping pelvic pain syndromes, and co-occurring psychiatric disorders were subject to a partition around medoids clustering to identify patient profiles. Profiles were compared across social history and subsequent treatment modality, prescribed medications, and surgeries performed. **Results:** Two profiles with equal proportion were identified. Profile 1 was vulvodynia and myofascial pelvic pain-dominant characterized by lower pain burden and better psychological functioning. Profile 2 was visceral pain-dominant featuring higher pain interference and catastrophizing, lower pain acceptance, and higher psychiatric comorbidity. Patients in Profile 2 had 2-4 times higher prevalence of childhood and adulthood abuse history ( $P_s < 0.001$ ), were more likely to subsequently receive behavioral therapy (46% vs 27%,  $P = 0.005$ ) and hormonal treatments (34% vs 21%,  $P = 0.04$ ), and were prescribed more classes of medications for pain management ( $P = 0.045$ ) compared to patients in Profile 1. **Conclusions:** Treatment-seeking women with CPP could be separated into two groups distinguished by pain clusters, pain burden, pain distress and coping, and co-occurring mental health disorders.



## **Approach to Diagnosis and Management of Chronic Pelvic Pain in Women: Incorporating Chronic Overlapping Pain Conditions in Assessment and Management**

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Chronic pelvic pain (CPP) is multifactorial in etiology and heterogeneous in presentation. Identification of all pain contributors is essential for successful management. Chronic overlapping pain conditions (COPCs) are a specified group of chronic pain conditions that commonly co-occur in patients. We briefly review individual COPCs and highlight risk factors and mechanisms that appear to be applicable across COPCs. We review evaluation and communication strategies that may help establish a productive therapeutic relationship between clinicians and patients. Management should include treatment of peripheral pain generators as well as co-occurring psychological conditions and central sensitization when present.

## **Persistent Genital Arousal Disorder**

### **Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia caused by Sacroiliac Joint Dysfunction**

Yunxu Zhang, Li Su, Hong Ge, Qiang Wang

Sex Med. 2022 Jul 15;10(5):100544. doi: 10.1016/j.esxm.2022.100544.

<https://pubmed.ncbi.nlm.nih.gov/35849889/>

**Introduction:** Persistent genital arousal disorder/genito-pelvic dysesthesia (PGAD/GPD) consists of persistent or recurrent unwanted sensations of genital arousal that may include other types of genito-pelvic dysesthesia, which occur without concomitant sexual interest or thoughts. There are multiple triggering factors for PGAD/GPD. **Aim:** To report the case of a 38-year-old woman with low back pain and PGAD/GPD triggered by sacroiliac joint dysfunction. **Methods:** The medical data of the female patient with low back pain and PGAD/GPD were reviewed and analyzed. **Results:** Resetting of the subluxated sacroiliac joint resulted in complete remission of the patient's symptoms.

**Conclusion:** Sacroiliac joint dysfunction may be a trigger for PGAD/GPD in some cases. Lack of relevant knowledge among patients and healthcare providers is the biggest challenge of the proper diagnosis and treatment of PGAD/GPD at present.

### **Lamotrigine-Induced Persistent Genital Arousal Disorder and a Potential Treatment**

Serena Suwarno, Samhita Vedula, Neet Shah, Kim Artounian, Alena Petty

J Sex Marital Ther. 2022 May 14;1-3. doi: 10.1080/0092623X.2022.2073931.

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Persistent Genital Arousal Disorder (PGAD) is a rare disorder characterized by involuntary genital arousal without relief after orgasm or subjective feelings of sexual excitement. There is sparse data for effective treatments of PGAD, which can cause significant distress, anxiety, and depression for patients. We present a case of a patient with major depressive disorder (MDD) and post-traumatic stress disorder (PTSD) who was diagnosed with PGAD shortly after she was started on lamotrigine for mood stabilization. Inpatient psychiatric treatment with increasing doses of sertraline resulted in reduction of her symptoms, suggesting its possible role in PGAD treatment and management.

### Sacral Nerve Stimulation in Patients With Refractory Pudendal Neuralgia

Kai-Kai Guo, Long Wang, Fang Liu, Jie-Jie Niu, Chao Wang, Shao-Hua You, Ze-Guo Feng, Gui-Jun Lu  
Pain Physician. 2022 Jul;25(4):E619-E627.

<https://pubmed.ncbi.nlm.nih.gov/35793186/>

**Background:** Pudendal neuralgia (PN) is one of the most common forms of genital pain. Only 42.2% of PN patients respond to the first-line treatment. Novel neuromodulation techniques in the treatment of refractory PN patients are urgently required. **Objectives:** The aim of this study was to evaluate the treatment effects and adverse events of sacral nerve stimulation (SNS) for patients with refractory PN. **Study design:** A prospective nonrandomized study. **Setting:** This prospective analysis included 33 patients who received the phase II surgical implantation. **Methods:** A total of 55 eligible PN patients were recruited for SNS treatment after informed consent, and 33 of 55 patients with a minimum 50% improvement were candidates for surgical implantation. Visual Analog Scale (VAS) scores, Self-rating Anxiety and Depression Scale, Quality of life score (SF-36), and sleep monitoring indicators before and after surgery were used to assess the effects of SNS on patients with refractory PN. **Results:** Thirty-three patients were included in the final analysis, involving 24 women and 9 men with a mean age of 49.5 years (26-70 years). There was a favorable decrease in pain severity (VAS scores) from  $7.1 \pm 1.1$  at baseline to  $6.1 \pm 1.0$  on postoperative day 1, and  $2.8 \pm 0.7$  at 1 week,  $1.7 \pm 0.5$  at 1 month,  $1.1 \pm 0.7$  at 6 months, and  $1.0 \pm 0.6$  at 12 months after surgery, respectively ( $P < 0.05$ ). The mean score of each section of SF-36 after SNS was significantly higher than that at baseline ( $P < 0.05$ ). Total sleep time and sleep time in each period were significantly prolonged after SNS implantation compared with that before surgery (6 months vs Pre, total:  $5.32 \pm 1.49$  hours vs  $3.66 \pm 1.19$  hours, deep:  $2.52 \pm 0.63$  hours vs  $1.36 \pm 0.43$  hours, light:  $1.78 \pm 0.42$  hours vs  $0.99 \pm 0.30$  hours, rapid eye movement:  $1.41 \pm 0.29$  hours vs  $0.89 \pm 0.27$  hours,  $P < 0.05$ ). No serious device complications were reported during the follow-up period. **Limitations:** Large-scale randomized clinical trials are warranted to evaluate the risk factors for prediction of refractory PN. **Conclusions:** These data imply that SNS can have beneficial effects on patients with refractory PN.

### When and How to Utilize Pudendal Nerve Blocks for Treatment of Pudendal Neuralgia

Abigail Cain, Kimberly Carter, Christina Salazar, Amy Young  
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<https://pubmed.ncbi.nlm.nih.gov/35703212/>

Chronic pelvic pain is a common cause of pain in reproductive age women with debilitating consequences for affected women's health and quality of life. Treatment providers must be well versed in all treatment options for these patients, understanding the overlap in the management and treatment of chronic pelvic pain caused by pudendal neuralgia, myofascial pelvic pain, and vulvodynia. Pudendal blocks are a simple and quick procedure that can be performed in the office and often helps improve all the above conditions when used along with other treatment options. We review the anatomy and methodology on when and how to perform pudendal blocks in the office to better inform the general gynecologist on how to implement offering this treatment in the outpatient clinical setting.

## **Nervus pudendus idegblokáád alkalmazása krónikus kismencedei fájdalmat okozó pudendusneuralgia kezelésében**

Miklós Romics, Orsolya Oláh, Kristóf Perczel, Barbara Petra Kovács, Dániel Milanovich, Éva Pintér, Péter Ónody, Attila Majoros

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Pudendal neuralgia is a rare and - in the absence of somatic, radiological and laboratory abnormalities - often unrecognizable problem, posing a serious challenge to therapeutic management. Our case study presents the complete diagnostic and therapeutic algorithm of a female patient with chronic pudendal pain. In addition, our paper draws attention to the role of pelvic pain workgroups - such as the Pelvic Pain Task Force of the Semmelweis University - where cases of chronic pelvic pain with no clear medical reason can be assessed and treated with higher efficiency.

## **Dermatological Conditions**

### **High-frequency ultrasound features in vulvar lichen sclerosus and correlation with histopathology**

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Skin Res Technol. 2022 Aug 15. doi: 10.1111/srt.13198.

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**Background:** Vulvar lichen sclerosus (VLS) is a chronic inflammatory disease initially involving anogenital areas. Noninvasive assessment is essential for precise management in VLS. We aim to analyze high-frequency ultrasound (HFUS) features and correlate HFUS with histopathological changes.

**Materials and methods:** Forty patients with histopathologically confirmed VLS lesions were retrospectively identified from August 2020 to September 2021. The clinical manifestations, dermoscopic images as well as both 20 and 50 MHz HFUS images were assessed. HFUS assessment included epidermal morphology, hypoechoic dermal band thickness, and hypoechoic dermal band internal echo. We compared HFUS images with histopathology, and Pearson's correlation coefficient was used to assess the relationship between hypoechoic dermal band thickness and histopathological depth. **Results:** Hypoechoic dermal band was present in 100% (40/40) VLS lesions. There was a significant linear positive correlation between the histopathological depth and corresponding hypoechoic dermal band thickness, with a Pearson correlation coefficient of 0.685 ( $p < 0.001$ ). Besides, 95% (38/40) lesions revealed smooth epidermis, and the internal echo of hypoechoic dermal band was assessed as homogeneous in 60% (24/40) and inhomogeneous in 40% (16/40) lesions. **Conclusion:** HFUS characteristics, as well as measurable hypoechoic dermal band thickness, may provide valuable information in the precise diagnosis and the treatment monitoring of VLS.

### **Prevalence and risk factors of vulvar dermatoses: A hospital-based study**

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**Background:** The overall prevalence of vulvar diseases in the literature is low because of underreporting and is often neglected; thus, its impact on a female's life is often underestimated. **Objectives:** This study is aimed to determine the prevalence of vulvar diseases and their associated risk factors in patients attending a tertiary care hospital. **Materials and methods:** This is a descriptive, cross-sectional, and case-controlled study wherein all female patients attending the dermatology outpatient department (OPD) were screened for the signs and symptoms of vulvar dermatoses and were enrolled after obtaining informed consent and institutional ethics committee approval for 21 months. Out of them, 200 patients who consented and had signs and symptoms of vulvar diseases were selected as cases, and the same number of age-matched females were enrolled as controls with no signs and symptoms of vulvar dermatoses. **Results:** During the study period, 9431 females attended the dermatology OPD, of which the prevalence was 2.12% (200 patients). The most common infection was genital infection without sexually transmitted infection (57%) (tinea cruris [33.5%]), followed by inflammatory dermatoses (21%) (lichen sclerosus et atrophicus [6%]). The most common risk factor found statistically significant ( $P \leq 0.005$ ) were homemakers (49%) and the use of undergarments of mixed fabric (70.68%), followed by nonmenopausal females (63.15%). **Conclusion:** Our study findings indicated that the prevalence was low, which reflects the tip of an iceberg. Further clinical and population-based studies, a multidisciplinary approach including gynecological consult for diagnostic and therapeutic approach is needed for the optimal management of vulvar diseases.

#### **High-intensity focused ultrasound therapy for pediatric and adolescent vulvar lichen sclerosis**

Sili He, Jianfa Jiang

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**Objective:** The study's objective was to retrospectively evaluate the efficacy and safety of high-intensity focused ultrasound (HIFU) for vulvar lichen sclerosis (VLS) in pediatric and adolescent patients.

**Methods:** Pediatric and adolescent patients presenting to our hospital from June 2007 to July 2021, with VLS were retrospectively evaluated. The participants' information, including age, symptoms and vulvar examination, were documented, and they were treated with HIFU. The effectiveness of HIFU and its complications were analyzed. **Results:** A total of 36 patients with VLS undergoing HIFU for whom complete follow-up data were available participated in the study. The mean age of the patients at diagnosis was  $13.3 \pm 4.1$  years. All patients successfully underwent HIFU therapy. The mean sonication time was  $20.3 \pm 8.6$  min, and the median treatment energy was 3579.0 J. A few blisters developed in 8 (22.2%) patients and 2 (5.6%) had ulcers. The skin burns were treated medically without scar formation. On average, patients were followed up for 52.0 months after the procedure (a range of 6-175 months). At 6 months after therapy, the total response rate was 91.6%, and 86.6% at 12 months post HIFU. Overall, 16 patients were followed up for more than 5 years. The total response rate was 75%, and the recurrence rate was 12.5%. **Conclusions:** Based on our results, HIFU was demonstrated to be effective and relatively safe for the treatment of VLS in pediatric and adolescent patients, but it is necessary to pay attention to the possible skin burns.

#### **Screening differential circular RNAs expression profiles in Vulvar Lichen Sclerosis**

Min Yang, Kailv Sun, Jianmin Chang

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**Background:** Vulvar lichen sclerosus (VLS) is one of the most common clinical manifestations of vulva. Thirteen percent of women have symptomatic vulvar diseases. The aim of this study is to investigate the expression profile of circular RNA (circRNAs) in vulvar lichen sclerosus, and to identify the underlying core genes of VLS. **Methods:** We removed rRNA for sequencing, and screened the differentially expressed messenger RNA (mRNAs), long non-coding RNA (lncRNAs) and single-stranded circRNA in 20 groups of VLS tissues and 20 groups of healthy female vulvar skin tissues. Bioinformatics analysis was used to analyze its potential functions. **Results:** A total of 2545 differentially expressed mRNAs were assessed in VLS patients, of which 1541 samples were up-regulated and 1004 samples were down-regulated. A total of 1453 differentially expressed lncRNAs were assessed, of which 812 samples were up-regulated and 641 samples were down-regulated. A total of 79 differentially expressed circRNAs were assessed, of which 54 were up-regulated and 25 were down-regulated. The differential expression of circRNAs was closely related to biological processes and molecular functions. The differences in circRNAs were mainly related to the "human T-cell leukemia virus 1 infection" signaling pathway and the "axon guidance" signaling pathway. **Conclusion:** The profile of abnormal regulation of circRNA exists in VLS. According to biological informatics analysis, the dysregulation of circRNAs may be related to the pathogenesis and pathological process of VLS.

### **Multiphoton microscopy assessment of the structure and variability changes of dermal connective tissue in vulvar lichen sclerosus: A pilot study**

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<https://pubmed.ncbi.nlm.nih.gov/35652856/>

In this article, we offer a novel classification of progressive changes in the connective tissue of dermis in vulvar lichen sclerosus (VLS) relying on quantitative assessment of the second harmonic generation (SHG) signal received from formalin fixed and deparaffinized tissue sections. We formulate criteria for distinguishing four degrees of VLS development: Initial-Mild-Moderate-Severe. Five quantitative characteristics (length and thickness type I Collagen fibers, Mean SHG signal intensity, Skewness and Coherence SHG signal) are used to describe the sequential degradation of connective tissue (changes in the structure, orientation, shape and density of collagen fibers) up to the formation of specific homogeneous masses. Each of the degrees has a characteristic set of quantitatively expressed features. We focus on the identification and description of early, initial changes of the dermis as the least specific. The results obtained by us and the proposed classification of the degrees of the disease can be used to objectify the dynamics of tissue changes during treatment.

### **Transcriptome Profiling and Network Analysis Provide Insights Into the Pathogenesis of Vulvar Lichen Sclerosus**

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Front Genet. 2022 Jun 17;13:905450. doi: 10.3389/fgene.2022.905450. eCollection 2022.  
<https://pubmed.ncbi.nlm.nih.gov/35783265/>

Vulvar lichen sclerosus (VLS) is a chronic inflammatory dermatosis that affects female anogenital skin. Although VLS is considered a T cell-mediated autoimmune disease, the diagnosis criteria, molecular mechanism, and universally accepted therapies for this disease remain largely unresolved. To explore

disease pathogenesis and potential biomarkers, we performed an RNA-Seq-based transcriptome analysis to profile the gene expression of VLS lesions. Differentially expressed gene (DEG) analysis revealed profound changes in expressions of coding genes, microRNAs, and long non-coding RNAs. Pathway and network analysis suggested that T cell activation-associated genes, including *CD3G*, *CD3D*, *CD8B*, *LAT*, *LCK*, *ZAP70*, *CCR5*, *CXCR3*, *CXCL9*, *CXCL10*, and *CXCL11*, were highly expressed in VLS, while *NR4A* family genes (*NR4A1*, *NR4A2*, *NR4A3*), whose coding products inhibit T cell activity, were significantly downregulated, suggesting heightened T cell response in VLS. Neutrophil chemoattractant genes *CXCL1*, *CXCL2*, *CXCL3*, *CXCL8*, and their cognate receptor *CXCR2* were downregulated, suggesting dampened neutrophil activity. We also found the downregulation of genes involved in cell cycle progression, including cyclins (*CCNB1*, *CCNB2*, *CCNL1*, *CCNE1*, and *CCNK*) and centrosome factors (*CENPA*, *CENPE*, *CENPF*, and *CENPN*), while microRNA-203a and let-7, microRNAs known to inhibit cell growth, were found to be upregulated. These data collectively indicate that cell proliferation in VLS is compromised. In sum, these findings comprehensively deciphered key regulatory genes and networks in VLS, which could further our understanding of disease mechanisms and point toward therapeutic strategies.

### **Comorbid Vulvar Lichen Sclerosus and High-Grade Squamous Intraepithelial Lesions: A Management Conundrum**

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<https://pubmed.ncbi.nlm.nih.gov/35972920/>

**Objective:** This study aimed to determine if treating lichen sclerosus (LS) with high-potency topical corticosteroids (TCS) increases the risk of high-grade squamous intraepithelial lesion (HSIL) recurrence in patients with comorbid vulvar LS and HSIL. **Methods:** This is a retrospective study of patients with comorbid vulvar LS and HSIL treated with TCS between 2015 and 2020. Patients with clinically diagnosed or biopsy-proven LS and biopsy-proven HSIL of the vulva were included. Clinical data included demographics, tobacco use, immune-modifying conditions, specimen pathology, treatment types, and HSIL recurrence. Bivariate analysis was performed to compare demographic and clinical characteristics between patients with and without HSIL recurrence. **Results:** Twenty-six patients with comorbid LS and HSIL were identified. The median age was 66.0 years and median time in treatment for LS was 5.5 years. Thirteen (50%) had recurrence of HSIL and 13 (50%) did not have recurrence. Exposure to high-potency TCS was present in 20 (77%) patients, with 17 (65%) having use of more than 1-year duration and 9 (35%) having use at the time of HSIL diagnosis. When comparing the groups with and without HSIL recurrence, there was no significant difference in high-potency TCS exposure, duration of use, or use at time of HSIL diagnosis. **Conclusions:** High-potency TCS use for the treatment of LS did not seem to increase the risk of HSIL recurrence in patients with comorbid vulvar LS and HSIL. This suggests that high-potency TCS can be appropriately used for the treatment of LS even when HPV-associated disease is present.

## Chinese expert consensus on the clinical applications of aminolevulinic acid-based photodynamic therapy in female lower genital tract diseases (2022)

Lihua Qiu, Jingran Li, Fei Chen, Yifeng Wang, Yue Wang, Xinyu Wang, Qiubo Lv, Changzhong Li, Mingzhu Li, Qiuyun Yang, Dan Wu, Youzhong Zhang, Yuquan Zhang, Mengzhen Zhang, Yu Zhang, Mingrong Qie, Huaijun Zhou, Jiade Zhou, Weidong Zhao, Bairong Xia, Xuefang Liang, Yunlang Cai, Yincheng Teng, Zheng Huang, Long Sui, Lihui Wei, Wen Di

Photodiagnosis Photodyn Ther. 2022 Jul 1;39:102993. doi: 10.1016/j.pdpdt.2022.102993.

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**Introduction:** With the younger onset age of female lower genital tract diseases, there are increasing demands for protecting organ and tissue structures to preserve fertility and, therefore, effective fertility-sparing treatments that cause minimal normal tissue damage and less adverse reactions are urgently needed. **Objective:** This study is aimed at reviewing information and achieving consensus on recommendations on the clinical applications of aminolevulinic acid-based photodynamic therapy (ALA-PDT) in female lower genital tract diseases. **Methods:** Members of the expert panel held online and in-person meetings to discuss and revise drafts created by the steering committee based on the literature review and the clinical experiences of the expert panel. Opinions of the experts were transcribed and discussed in detail to ensure that the consensus statement best reflects the current advances in the field and the experts' view. **Results:** After numerous rounds of meetings, experts unanimously agreed on the importance of ALA-PDT in the treatment of cervical squamous intraepithelial lesions (SIL), vaginal SIL, vulvar SIL, vulvar lichen sclerosus (VLS), and condyloma acuminatum (CA). Experts also reached consensus on the recommended treatment regimen and treatment methods. **Conclusion:** This consensus aimed to provide practical basis and guidance for the clinical applications of ALA-PDT in female lower genital tract diseases in China. Of note, this is the only expert consensus prepared by board-certified specialists in gynecology and obstetrics in China. More evidence-based clinical studies should be made to update and expand the current recommendations.

## The Impact of Psychosexual Counseling in Women With Lichen Sclerosus: A Randomized Controlled Trial

[Article in Danish, English]

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**Introduction:** Lichen sclerosus (LS) can affect sexuality and quality of life (QoL). **Objective:** The aim of the study was to evaluate the impact of psychosexual counseling in women with LS. **Materials and methods:** One hundred fifty-eight women 18 years or older, newly diagnosed with LS, and referred to North Denmark Regional Hospital from January 2018 to November 2019 were included. The women were randomized in a 1:1 ratio to usual care or an intervention group receiving usual care and up to 8 individual consultations with a specialist in sexual counseling. Spouses or partners were encouraged to participate. The women filled out the questionnaires Female Sexual Function Index (FSFI), Dermatology Life Quality Index, and the WHO-5 Well-Being Index at baseline and after 6 months. **Results:** The controls presented a mean score of  $14.8 \pm 8.7$  and the intervention group presented a mean score of  $12.8 \pm 8.9$  at FSFI. At follow-up, the controls had an FSFI score of  $15.2 \pm 9.2$  and the intervention group revealed an FSFI score of  $18.3 \pm 9.5$ . Both groups experienced improved sexual functioning and for the

intervention group the increase was significant ( $p < .001$ ). At baseline, the Dermatology Life Quality Index mean score was  $8.9 \pm 5.6$  for the control group and  $9.3 \pm 6.1$  for the intervention group. At follow-up, the controls revealed a score of  $8.6 \pm 5.5$  and the intervention group a score of  $6.8 \pm 5.8$ . The intervention group reached a significantly higher degree of QoL than the controls ( $p = .008$ ).

**Conclusions:** Psychosexual counseling has a significant impact on sexual functioning and QoL in women with LS.

### **Genital Self-Image, Sexual Function, and Quality of Life Among Individuals with Vulvar and Non-Vulvar Inflammatory Dermatoses**

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Vulvar inflammatory dermatoses (VID; e.g., lichen sclerosus, lichen planus, vulvar dermatitis) can significantly impact sexual function. Both vulvar and non-vulvar inflammatory dermatoses (NVID; i.e., skin conditions not impacting vulvar skin, such as non-genital psoriasis and eczema/dermatitis) have yet to be fully characterized with regard to impact on genital self-image. A 20-min web-based survey was distributed September–November 2020 through social media ads, support groups, and online research recruitment services. Individuals in the USA over age 18 who were assigned female at birth and self-reported having been diagnosed with an inflammatory dermatosis were eligible. The primary outcome was the Female Genital Self-Image Scale (FGSIS). Secondary outcomes included the Female Sexual Function Index (FSFI), the Skindex-16 (a skin-related quality of life measure), the PROMIS Global-10 (assessing global physical/mental health), and sexual behavior histories. Participants ( $n = 348$ ) reported mean age of  $43.1 \pm 15.5$  (range = 19–81). Nearly one-third ( $n = 101$ ; 29.0%) reported VID, 173 (50%) had NVID, and 74 (21%) experienced both vulvar and non-vulvar symptoms; they were analyzed as part of the VID group. The mean FGSIS score among participants with VID was  $16.9 \pm 4.1$  and was significantly ( $p < .01$ ) lower than that of participants with NVID ( $M = 21.2 \pm 4.3$ ), indicating lower genital self-image. Mental health (as measured by PROMIS-Global 10) was also impaired in VID. Rates of sexual dysfunction were high in both groups ( $> 60\%$ ). Findings suggest that in VID, lower genital self-image is correlated with poorer sexual function, quality of life, and global physical and mental health. Additional recommendations for VID management are proposed.