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Vulvodynia

Cytokine profiles of women with vulvodynia: Identification of a panel of pro-inflammatory molecular targets.

Zanotta N, Campisciano G, Scrimin F, Blendi U, Marcuzzi A, Vincenti E, Crovella S, Comar M.
Eur J Obstet Gynecol Reprod Biol. 2018 Jul;226:66-70. doi: 10.1016/j.ejogrb.2018.05.035. Epub 2018 May 24.

<https://www.ncbi.nlm.nih.gov/pubmed/29852336>

OBJECTIVE: The vulvar pain syndrome (VPS) is a multifactorial disease severely influencing the lifestyle of affected women. Among possible etiological factors, local injury, peripheral and/or central sensitization of the nervous system, and a chronic inflammatory status have been positively associated with the development of VPS. The identification of a constitutive altered local inflammatory profile in VPS women may represent an important point in the characterization of patients' phenotype as a useful marker influencing the vulvar micro-environment. The aim of this study was to investigate the possible role of the local cytokines production in women with VPS in comparison to healthy women.

STUDY DESIGN: In this study were collected vaginal swabs from 57 healthy women (HC) who never suffered from VPS and from 30 patients diagnosed with vulvodynia (VPS) by at least 3 years and currently symptomatic. All patients included in this study showed the absence of Sexually Transmitted (STD) diseases and Reproductive Tract Infection. Real-time PCR was performed to assess the genomic sequences of ST pathogens. The Luminex Bio-Plex platform was used for the analysis of a panel of 48 immune factors. **RESULTS:** Eleven molecules, specifically involved in the pro-inflammatory pathway were significantly modulated in VPS patients in comparison to healthy women, suggesting a persistent inflammatory process. **CONCLUSIONS:** Therefore, these inflammatory factors could be possible biological markers involved in this disease. Nevertheless, other studies are needed to consider this specific immune profile as a valid marker of the vulvodynia.

Nerve Growth Factor and Selected Cytokines in Women With and Without Vulvodynia.

Reed BD, Plegue MA, Sen A, Haefner HK, Siddiqui J, Remick DG.

J Low Genit Tract Dis. 2018 Apr;22(2):139-146. doi: 10.1097/LGT.0000000000000377.

<https://www.ncbi.nlm.nih.gov/pubmed/29570566>

OBJECTIVE: The aim of the study was to assess the association between cytokines/neurokines after in vitro stimulation with Candida antigen or lipopolysaccharide (LPS) in blood samples among women with and without vulvodynia. **MATERIALS AND METHODS:** Women with vulvodynia and asymptomatic controls at three offices at the University of Michigan were examined clinically and completed a comprehensive survey in this cross-sectional study. Cytokine/neurokine levels were determined on blood samples using established ELISA protocols. Analysis of 48 cases and 42 ethnically matched controls included descriptive statistics (median, minimal, and maximal levels of cytokines/neurokines), overall and in cases and controls. Because of left-censored measurements, interval censored survival analysis was used to assess the association between case/control status and pain characteristics with cytokine/neurokine levels. **RESULTS:** Participants ranged in age from 19 to 60 years. Levels of IL1 β , IL1-RA, TNF α , IL-6, and IL-8 increased substantially after LPS stimulation, whereas no response was seen on IFN γ or nerve growth factor (NGF). Each increased after Candida antigen stimulation, although responses to Candida antigen stimulation of IL1 β , IL-6, and TNF α were less robust than after LPS. Only NGF was significantly increased in vulvodynia cases compared with controls (Exp β (95% CI) = 2.08 [1.08-3.98]) after 24-hour Candida antigen stimulation and persisted when controlled for age, use of oral contraceptives, or history of Candida vulvovaginitis. No association between cytokine/neurokine levels and pain characteristics was found. **CONCLUSIONS:** Compared with that of control women, whole blood from women with vulvodynia demonstrates an enhanced production of NGF, but not of a set of inflammation-related cytokines, in response to Candida antigen stimulation.

Double-blind acupuncture needles: a multi-needle, multi-session randomized feasibility study.

Schlaeger JM, Takakura N, Yajima H, Takayama M, Steffen AD, Gabzdyl EM, Nisi RA, McGowan Gruber K, Bussell JM, Wilkie DJ.

Pilot Feasibility Stud. 2018 Apr 13;4:72. doi: 10.1186/s40814-018-0265-9. eCollection 2018.

<https://www.ncbi.nlm.nih.gov/pubmed/29686883>

BACKGROUND: Efficacy of acupuncture is difficult to demonstrate without a feasible double-blind milieu. Double-blind acupuncture needles have been validated in single session protocols with one or two needles but not been tested in a protocol requiring many needles and repeated sessions.

METHODS: We determined the feasibility of a 13-needle, 10-session study protocol. Feasibility focused on (1) enrolling and retaining participants; (2) two acupuncturists accurately implementing a double-blind, multi-needle, multi-session protocol; (3) participants completing measures; and (4) protocol acceptability to participants. In this double-blind randomized controlled pilot study, participants were randomized 1:1 to a penetrating needle group or a skin-touch placebo control group. **RESULTS:** Six women with vulvodynia (mean age 31.5 \pm 8 years; five white, non-Latina, one black/African American) met the eligibility requirements, consented to participation, and were enrolled. All six participants (100%) completed the 10-session study protocol in 5 weeks without missing any treatment sessions. Per observed checklist documented technique, two acupuncturists flawlessly administered the 13-needle, 10-session acupuncture protocol; no needles malfunctioned. Six participants attended all sessions and completed 99% of measurement items. One participant did not like acupuncture (60% acceptability score) and five liked acupuncture (100% acceptability scores); the mean acceptability score was 93.3%. **CONCLUSION:** Study feasibility was supported. This protocol can be used in a double-blind

efficacy trial of acupuncture for vulvodynia. **TRIAL REGISTRATION:** ClinicalTrials.gov, [NCT02704234](https://clinicaltrials.gov/ct2/show/study/NCT02704234). Registered 30 November 2015.

Patterns in Vulvodynia Treatments and 6-Month Outcomes for Women Enrolled in the National Vulvodynia Registry-An Exploratory Prospective Study.

Lamvu G, Alappattu M, Witzeman K, Bishop M, Robinson M, Rapkin A.

J Sex Med. 2018 May;15(5):705-715. doi: 10.1016/j.jsxm.2018.03.003. Epub 2018 Apr 7.

<https://www.ncbi.nlm.nih.gov/pubmed/29631955>

BACKGROUND: Vulvodynia is a poorly characterized condition with multiple treatment options that have been described as largely ineffective in research settings. **AIM:** To describe treatment patterns in women enrolled in the National Vulvodynia Registry and determine if there is an association between selected treatments and patient-reported outcomes such as pain, sexual function, and psychological distress after 6 months of treatment. **METHODS:** Participants completed questionnaires on general medical history and patient-reported outcomes using the short-form McGill Pain Questionnaire, the Female Sexual Function Index, the Short Form-12 quality-of-life questionnaire, the Coping Strategies Questionnaire, and the State-Trait Anxiety Inventory. The evaluation also included pain sensitivity assessment of the vaginal mucosa using a cotton-tipped applicator and the vaginal muscles using a single-digit. In this prospective cohort study, all measurements were collected at baseline and again at 6 months after treatment. **OUTCOMES:** Type of treatment, number of treatments, self-reported pain intensity, dyspareunia, and pain-related psychological distress measures are reported at baseline and 6 months. **RESULTS:** Of 344 women enrolled, 282 received treatment; 78 different treatments were identified and categorized by type (eg, topical, oral, physical therapy) and number. The most commonly used treatments were topical (85%, n = 241), physical therapy (52%, n = 147), and oral medications (45%, n = 128). Notably, 73% of participants received ≥ 2 treatments. There was no association between type or number of treatments and patient characteristics. At 6 months, women reported improvements in general pain ($P = .001$), pain during intercourse ($P = .001$), catastrophizing ($P = .000$), and anxiety ($P = .000$). The Short Form-12 quality-of-life questionnaire showed improvements in physical limitations ($P = .024$), emotional limitations ($P = .003$), well-being ($P = .025$), and social function ($P = .010$). However, all domains of the Female Sexual Function Index indicated worsening in sexual function ($P = .000$) except for pain. **CLINICAL TRANSLATION:** Multi-modal treatments were most commonly used in clinical practice and improvements in patient-reported outcomes such as quality of life, distress, and pain were noted; however, participants who returned at 6 months continued to report poor sexual function. **CONCLUSIONS:** Strengths include a prospective and long-term study design that evaluated women in clinical settings. Limitations include a high rate of loss to follow-up for certain measures and inability to evaluate efficacy of individual treatments. In a setting where women were receiving highly specialized care, we found wide variation in the type and number of treatments used to treat vulvodynia. Despite this heterogeneity in treatment selection, women reported significant improvements in all study measures except sexual function. Lamvu G, Alappattu M, Witzeman K, et al. Patterns in Vulvodynia Treatments and 6-Month Outcomes for Women Enrolled in the National Vulvodynia Registry-An Exploratory Prospective Study.

Antenatal Vulvar Pain Management, Labour Management, and Postpartum Care of Women With Vulvodynia: A Survey of Physicians and Midwives.

Smith KB, Basson R, Sadownik LA, Isaacson J, Brotto LA.

J Obstet Gynaecol Can. 2018 May;40(5):579-587. doi: 10.1016/j.jogc.2017.09.014.

<https://www.ncbi.nlm.nih.gov/pubmed/29731205>

OBJECTIVE: To examine maternity providers' recommendations for pregnant women with vulvodynia regarding management of vulvar pain and postpartum care, and to examine if, and how, a woman's chronic vulvar pain affects providers' examination and management during labour. **METHODS:** This research was part of a larger study that invited physicians and midwives to answer a questionnaire regarding pregnancy and childbirth care in women with vulvodynia. To achieve the current objectives, the questionnaire included both dichotomous (yes or no) and open-ended items. The current sample (n = 116) consisted of 75 physicians and 41 midwives. **RESULTS:** Over 60% of the sample reported making recommendations for vulvar pain management during pregnancy, and 32.8% of providers reported making special postpartum care recommendations for women with vulvodynia. Differences between physicians and midwives were noted for some of these recommendations. For example, to manage vulvar pain, only physicians recommended the use of/change in medications (P < 0.001) and only midwives recommended complementary medicines (P = 0.02) and the use of lubricants (P = 0.006) and made recommendations for sexual well-being (P = 0.02). The majority of the sample (75%) reported that a woman having vulvodynia affected labour examination and management; providers most frequently reported minimizing exams and early use of epidural. Over 80% of midwives and 54% of physicians minimized exams during labour for women with vulvodynia (P = 0.01). **CONCLUSION:** Further research is needed to understand the optimal provision of care for pregnant and postpartum women with vulvodynia. We advocate for increased education of vulvodynia aimed at providers of antenatal, labour, and postnatal care.

Vulvodynia and chronic pelvic pain in a gynecologic outpatient clinic.

Trutnovsky G, Plieseis C, Bjelic-Radisic V, BertholinyGalvez MC, Tamussino K, Ulrich D.

J Psychosom Obstet Gynaecol. 2018 May 31:1-5. doi: 10.1080/0167482X.2018.1477753.

<https://www.ncbi.nlm.nih.gov/pubmed/29848143>

INTRODUCTION: Vulvodynia and chronic pelvic pain are common but underdiagnosed chronic gynecologic pain syndromes. Insufficient knowledge regarding prevalence, typical pain patterns and associated factors contribute to delayed diagnosis. The present study explored the symptoms and characteristics of women presenting with vulvodynia and/or chronic pelvic pain to a gynecologic outpatient clinic. **MATERIALS AND METHODS:** Electronic charts of women diagnosed with vulvodynia and/or chronic pelvic pain between January 2010 and December 2015 were reviewed. Type of pain, duration of symptoms, previous medical assessments and therapies, comorbidities and patient characteristics were analyzed with descriptive statistics. **RESULTS:** One hundred and twenty-seven women (mean age 36, range 18-75 years) met the diagnostic criteria for chronic gynecologic pain syndromes. Sixty-five women were diagnosed with CPP only, 42 with vulvodynia and 20 with both conditions. Endometriosis was suspected or diagnosed in 35 (54%) women with CPP. History of pain ranged from 3 months to 20 years. Comorbidities were common, with 40% of women being diagnosed with depression or other mood disorders, 15% with urological and 9% with gastrointestinal conditions. **CONCLUSIONS:** There is a need for increased awareness regarding vulvodynia and CPP among health care providers. A comprehensive history is important for adequate diagnosis.

Early experience with topical meloxicam and lidocaine combination for the treatment of vulvodynia.

Kim R, Kelly KL, Olsen M, Nickel JC.

Can Urol Assoc J. 2018 Apr 6. doi: 10.5489/cuaj.4976.

<https://www.ncbi.nlm.nih.gov/pubmed/29629863>

INTRODUCTION: We report our early clinical observations on the use of topical meloxicam and lidocaine gel for patients with vulvodynia. **METHODS:** This is an early experience in participants with a history of vulvodynia evaluated and treated at the Queen's University Pelvic and Bladder Pain Clinic. Combination meloxicam 0.3% and lidocaine 5% were provided to the participants and they were instructed to apply 5 cc to the vulvar area twice daily. Standardized assessment was conducted for each participant before the start of the topical therapy and again at one week included Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), and pain scoring (Likert) for vulvar pain, in addition to a subjective global assessment after a week of treatment. **RESULTS:** Of the eight participants, six had a subjective improvement in their symptoms with the use of the combination gel. They reported between one- and four-point reductions on the Likert pain scale and mild to moderate improvement of symptoms. Common side effects reported were burning and stinging. **CONCLUSIONS:** The results from this early experience are promising for a potentially effective topical treatment for vulvodynia.

A systematic review of drug treatment of vulvodynia: evidence of a strong placebo effect.

Miranda Varella Pereira G, Soriano Marcolino M, Silveira Nogueira Reis Z, Vale de Castro Monteiro M.

BJOG. 2018 Mar 23. doi: 10.1111/1471-0528.15223.

<https://www.ncbi.nlm.nih.gov/pubmed/29569822>

BACKGROUND: Vulvodynia is the most common type of chronic pelvic pain and dyspareunia in premenopausal women. The effect of drugs for the treatment of vulvodynia remains poorly discussed. **OBJECTIVES:** To conduct a systematic review of randomised controlled studies which assess medications used to treat vulvar pain in vulvodynia. **SEARCH STRATEGY:** Web of Science, Cochrane Library, EBSCO Academic, LILACS and MEDLINE were searched from 1985 to September 2016. **SELECTION CRITERIA:** Randomised controlled trials comparing any kind of medication for vulvodynia treatment with placebo or with another medication in adult patients were included. **DATA COLLECTION AND ANALYSIS:** The two investigators independently conducted data extraction. The synthesis was provided by the pain reduction index. Study quality assessment was performed using the Cochrane Handbook for Systematic Reviews of Intervention and analysis of publication bias was conducted. **MAIN RESULTS:** Five studies were included in qualitative synthesis. Number of participants varied from 30 to 133 participants among the eligible studies, resulting in a total of 297 patients. The pain reduction rates of patients with vulvodynia assessed by Q-tipped cotton test and visual analogue scale varied between studies. Placebo was shown to be as effective as any medication. **CONCLUSIONS:** There is a need for further studies evaluating topical monotherapy for the treatment of vulvodynia, as they are the main drugs used in clinical practice. **TWEETABLE ABSTRACT:** No medication has shown impact on vulvar pain in vulvodynia. There is evidence of a placebo effect.

Sexual Cues Mediate the Daily Associations Between Interpersonal Goals, Pain, and Well-being in Couples Coping With Vulvodynia.

Rosen NO, Muise A, Impett EA, Delisle I, Baxter ML, Bergeron S.

Ann Behav Med. 2018 Feb 17;52(3):216-227. doi: 10.1093/abm/kax046.

<https://www.ncbi.nlm.nih.gov/pubmed/29538663>

BACKGROUND: Vulvodynia is an idiopathic vulvovaginal pain condition that has significant sexual and relational consequences. Most women with vulvodynia continue to have intercourse, possibly because of a desire to approach positive outcomes (e.g., intimacy) and avoid negative outcomes (e.g., partner disappointment). **PURPOSE:** This study examined daily associations between approach and avoidance sexual goals and women's pain during intercourse and couples' sexual and relational well-being, as well as the mediating role of sexual cues. **METHODS:** Over 8 weeks, on sexual activity days ($M = 8.77$), women with vulvodynia ($N = 101$) and their partners reported their sexual goals, attention to sexual cues, sexual function, and relationship satisfaction, and women reported pain during intercourse. **RESULTS:** On days when women and partners held higher approach goals, they attended more to positive sexual cues, and in turn, felt more relationally satisfied, whereas on days when they held higher avoidance sexual goals, partners were more focused on negative sexual cues, and in turn, partners reported lower relationship satisfaction. On days when women reported higher approach goals, they reported less pain, and both they and their partners attended more to positive sexual cues, and in turn, both had higher sexual function, whereas on days when women reported higher avoidance goals, both they and their partners attended more to negative sexual cues, and in turn, women reported greater pain, and both partners reported poorer sexual function. **CONCLUSIONS:** Interventions should target cognitive-affective processes during sexual activity as one pathway by which sexual goals impact pain and adjustment.

Evaluation and Treatment of Female Sexual Pain: A Clinical Review.

Sorensen J, Bautista KE, Lamvu G, Feranec J.

Cureus. 2018 Mar 27;10(3):e2379. doi: 10.7759/cureus.2379.

<https://www.ncbi.nlm.nih.gov/pubmed/29805948>

Dyspareunia and vulvodynia are genital pain disorders that have devastating effects on women's quality of life. These disorders occur with high prevalence and place a significant financial burden on women and the health care system. Many women do not report genital pain, and most providers do not inquire about this type of pain. As a result, women also experience social isolation. Numerous treatments are thought to improve quality of life and decrease pain; however, more studies are needed. This review aims to provide an overview of clinical evaluation methods and to summarize treatment options for women suffering from dyspareunia and vulvodynia.

Communal motivation in couples coping with vulvodynia: Sexual distress mediates associations with pain, depression, and anxiety.

Muise A, Bergeron S, Impett EA, Delisle I, Rosen NO.

J Psychosom Res. 2018 Mar;106:34-40. doi: 10.1016/j.jpsychores.2018.01.006. Epub 2018 Jan 10.

<https://www.ncbi.nlm.nih.gov/pubmed/29455897>

OBJECTIVE: To examine the role of a novel motivational perspective-sexual communal motivation-in women's pain during intercourse and both partners' distress in couples coping with vulvodynia, a prevalent gynecological pain condition. Our goal was to test whether sexual communal strength (i.e., motivation to meet a partner's sexual needs) and unmitigated sexual communion (i.e., prioritization of a partner's sexual needs in neglect of one's own needs) were indirectly associated with pain, depression, and anxiety via sexual distress. **METHODS:** Couples (N=101) completed daily surveys about their sexual communal motivation, sexual distress, anxiety, depression, and women reported on their pain during intercourse. Using multilevel modeling, we examined how daily fluctuations in sexual communal motivation were directly and indirectly (via sexual distress) associated with pain and psychological distress. **RESULTS:** On days when women with vulvodynia reported higher sexual communal strength, they reported less pain and anxiety, and on days when they reported higher unmitigated sexual communion, they reported more pain, more anxiety, and both partners reported more depressive symptoms. Daily associations between women's unmitigated sexual communion and greater pain, depression and anxiety were mediated by sexual distress. **CONCLUSIONS:** Being motivated to meet a partner's sexual needs was associated with less pain and anxiety for women with vulvodynia, but when this motivation excluded a focus on one's own needs, there were detrimental consequences for women's pain and both partners' depressive symptoms. Interventions for improving women's pain and the psychological well-being of affected couples should target motivational factors and sexual distress.

Provoked Vestibulodynia

Can maximal voluntary pelvic floor muscle contraction reduce vaginal resting pressure and resting EMG activity?

Naess I, Bø K.

Int Urogynecol J. 2018 Mar 12. doi: 10.1007/s00192-018-3599-1.

<https://www.ncbi.nlm.nih.gov/pubmed/29532122>

INTRODUCTION AND HYPOTHESIS: The purpose of the present study was to assess whether attempts at a maximal voluntary pelvic floor muscle (PFM) contraction can reduce vaginal resting pressure (VRP) and surface EMG activity in women with and without provoked vestibulodynia (PVD). **METHOD:** An assessor blinded comparison study included 35 women with and 35 women without PVD. VRP and PFM strength were measured with a high precision pressure transducer connected to a vaginal balloon (Camtech AS, Sandvika Norway). PFM activity was measured before and after three MVCs with surface EMG (NeuroTrac ETS™; Verity Medical, Romsey, UK). Paired sample t test was used to analyze differences within groups and independent sample t test to analyze differences between groups. p value was set at <0.05. **RESULTS:** Mean age of the participants was 24.3 years (SD 4.7) and mean BMI was 22.0 kg/m² (SD 2.6). There were no significant differences between the groups in any background variables. PFM contraction led to a statistically significant reduction of VRP in both the PVD (p = 0.001) and the control group (p = 0.027). Surface EMG activity was significantly reduced in the PVD group only (p = 0.001). **DISCUSSION:** Young, nulliparous women with PVD had significantly lower vaginal resting pressure and sEMG activity after three maximum contractions of the PFM. The results indicate that attempts at voluntary maximal contractions may be investigated as a method of reducing PFM hypertonicity.

Relationships Between 3-Dimensional Transperineal Ultrasound Imaging and Digital Intravaginal Palpation Assessments of the Pelvic Floor Muscles in Women With and Without Provoked Vestibulodynia.

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

J Sex Med. 2018 Mar;15(3):346-360. doi: 10.1016/j.jsxm.2017.12.017.

<https://www.ncbi.nlm.nih.gov/pubmed/29502982>

BACKGROUND: Digital intravaginal palpation remains the favored method for clinical assessment of pelvic floor muscle (PFM) function in women; however, there is growing interest in using transperineal ultrasound imaging (TPUSI). TPUSI does not involve vaginal penetration, making it particularly relevant for PFM assessment in women with genito-pelvic pain and penetration disorders. **AIMS:** To study the relations between measures of PFM morphology and function assessed using 3-dimensional (3D) TPUSI and PFM assessment through intravaginal palpation. **METHODS:** 77 nulliparous premenopausal women with (n = 38) and without (n = 39) PVD participated. 3D TPUSI was used to measure levator hiatus dimensions at rest, at maximal voluntary contraction (MVC) of the PFMs, and at maximal Valsalva maneuver (MVM). Intravaginal palpation was used to assess PFM strength, PFM tone, PFM relaxation after contraction, and vaginal flexibility; each was scored using an ordinal grading scale. Ultrasound and palpation outcomes were compared using Spearman correlation coefficients and Kruskal-Wallis 1-way analyses of variance by rank. **OUTCOMES:** Outcomes included ultrasound measures of the levator hiatus area, anteroposterior diameter, and left-right transverse diameter at rest, at MVC, and at MVM; raw and relative changes in hiatus dimensions between rest and MVC and between rest and MVM; and palpation measures of PFM strength, tone, and relaxation after contraction, and vaginal flexibility. **RESULTS:** Weak to fair correlations were found between ultrasound and palpation measures. A smaller levator hiatus at rest was associated with greater PFM tone, less PFM relaxation, and less vaginal flexibility. Greater levator hiatus constriction and shortening of the hiatus anteroposterior diameter at MVC were associated with greater palpated PFM strength. Greater hiatus distention at MVM was associated with lower PFM tone and greater relaxation. **CLINICAL TRANSLATION:** 3D TPUSI and intravaginal palpation provide related but distinct information about PFM function in young women with and without PVD with high functioning PFMs. **STRENGTHS AND LIMITATIONS:** This was the first study to compare PFM assessment using 3D TPUSI and intravaginal palpation in nulliparous premenopausal women. A main strength of the study was the inclusion of women with PVD and asymptomatic controls, which provided a wide range in outcomes because differences in PFM morphology and function exist between women with and without PVD. The lack of inclusion of older women and women with weaker and/or hypotonic PFMs limits the generalizability of the findings. **CONCLUSION:** Although TPUSI has several advantages, including painless application, it is not recommended as a replacement for digital palpation in the clinical assessment of PFM function. Thibault-Gagnon S, Goldfinger C, Pukall C, et al. Relationships Between 3-Dimensional Transperineal Ultrasound Imaging and Digital Intravaginal Palpation Assessments of the Pelvic Floor Muscles in Women With and Without Provoked Vestibulodynia.

Disease-Related Microstructural Differences in the Brain in Women With Provoked Vestibulodynia.

Gupta A, Woodworth DC, Ellingson BM, Rapkin AJ, Naliboff B, Kilpatrick LA, Stains J, Masghati S, Tillisch K, Mayer EA, Labus JS.

J Pain. 2018 May;19(5):528.e1-528.e15. doi: 10.1016/j.jpain.2017.12.269. Epub 2018 Jan 31.

<https://www.ncbi.nlm.nih.gov/pubmed/29391213>

Provoked vestibulodynia (PVD) is a chronic pelvic pain disorder affecting 16% of the female population. Neuroimaging studies have highlighted central abnormalities in PVD, similar to other chronic pelvic pain disorders, including brain regions involved in sensory processing and modulation of pain. The aim of the study was to determine alterations in the subvoxel, microstructural organization within tissues in PVD compared with healthy control participants (HCs) and a disease control group (irritable bowel syndrome [IBS]). Diffusion tensor imaging magnetic resonance imaging was conducted in 87 age-matched premenopausal women (29 PVD, 29 HCs, 29 IBS). Statistical parameter mapping of fractional anisotropy (FA) and mean diffusivity (MD) maps were used to identify microstructural difference in the brain specific to PVD or shared with IBS. PVD alterations in microstructural organization of the brain were predominantly observed in fibers associated with sensorimotor integration and pain processing that relay information between the thalamus, basal ganglia, sensorimotor, and insular cortex. PVD, compared with HCs, showed extensive increases in the FA of somatosensory and basal ganglia regions. In contrast, PVD and IBS subjects did not show any FA-related group differences. PVD subjects showed greater MD in the basal ganglia compared with HCs (higher MD in the internal capsule and pallidum) and IBS (higher MD in the putamen and pallidum). Increases in MD were associated with increased vaginal muscle tenderness and vulvar pain. The current findings highlight possible shared mechanisms between 2 different pelvic pain disorders, but also highlight the widespread alterations observed specifically in PVD compared with HCs. **PERSPECTIVE:** Alterations in microstructure in PVD were observed in fibers associated with sensorimotor integration and pain processing, which were also associated with increased vaginal muscle tenderness and vulvar pain. These alterations may be contributing to increased pain sensitivity and tenderness, highlighting the need for new therapies targeting the central nervous system.

Fear-avoidance and Pelvic Floor Muscle Function are Associated with Pain Intensity in Women with Vulvodynia.

Benoit-Piau J, Bergeron S, Brassard A, Dumoulin C, Khalifé S, Waddell G, Morin M.

Clin J Pain. 2018 Mar 9. doi: 10.1097/AJP.0000000000000604.

<https://www.ncbi.nlm.nih.gov/pubmed/29528864>

OBJECTIVE: To investigate the association between fear-avoidance variables, pelvic floor muscle (PFM) function and pain intensity in women with provoked vestibulodynia (PVD) as well as the moderator effect of partner support. **METHODS:** A total of 173 women diagnosed with PVD participated in the study. Fear-avoidance variables were evaluated with validated self-administered questionnaires: pain catastrophizing (Pain Catastrophizing Scale), pain-related fear (Pain Anxiety Symptoms Scale), and partner support (Partner Support Questionnaire). Pain intensity was evaluated using a numerical rating scale. PFM function, including maximal strength, speed of contraction, flexibility and muscle tone, was evaluated with a dynamometric speculum. **RESULTS:** Pain catastrophizing was significantly associated with pain intensity ($\beta=0.310$, $P<0.001$), as was partner support ($\beta=0.194$, $P=0.004$) and PFM flexibility ($\beta=-0.255$, $P<0.001$). Fear-avoidance, PFM variables and partner support explained 28.3% of the variance in pain during intercourse ($P<0.001$). The addition of PFM was of particular interest since it explained a significant addition of 9% in pain intensity. Partner support was found to moderate the association between pain intensity and catastrophizing. Among women with high partner support, catastrophizing was not significantly related to pain ($b=0.150$, $P=0.142$). When partner support was low, catastrophizing was significantly related to pain ($b=0.068$, $P<0.001$). **DISCUSSION:** Findings of this study support that the symptomatology of PVD can be explained partly by fear-avoidance variables and pelvic floor muscle function. This study supports the significant role of PFM function and its importance in the

pathophysiology of PVD. It also sheds light on the role of partner support and its moderating effect on pain catastrophizing.

Recovering from provoked vestibulodynia: Experiences from encounters with somatocognitive therapy.

Danielsen KG, Dahl-Michelsen T, Håkonsen E, Haugstad GK.

Physiother Theory Pract. 2018 Feb 23;1-10. doi: 10.1080/09593985.2018.1442540.

<https://www.ncbi.nlm.nih.gov/pubmed/29474104>

Although provoked vestibulodynia (PVD) represents a significant challenge for many young women in the Western world, little is known about how these women experience therapeutic efforts. The aim of this paper is to enhance our knowledge of the way that the therapeutic process is experienced by women with PVD undergoing somatocognitive therapy (SCT). The study enhances insight into this recently developed therapy through a detailed description of the physiotherapy approach. The empirical data are based on interviews with six women who participated in SCT. The empirical data analysis is guided by thematic analysis. Our findings demonstrate how the women experience SCT as a bodily process of wholeness. The process of wholeness relates to new experiences in the women's own bodies, awareness of muscular and mental tension and relaxation, breathing patterns, and perceptions focusing on pain. The findings are presented as three interrelated themes: 1) sensitizing the body as an interconnected unit; 2) incorporating the painful pubic region into the body; and 3) developing a new understanding of oneself. The women who participated in this study found that SCT contributed significantly to the process of their recovery from PVD.

Pain, psychological distress and motor pattern in women with provoked vestibulodynia (PVD) - symptom characteristics and therapy suggestions.

Haugstad GK, Wojniusz S, Kirste UM, Kirschner RS, Lilleheie I, Haugstad TS.

Scand J Pain. 2018 Apr 25;18(2):221-227. doi: 10.1515/sjpain-2017-0173.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Kirschner%20RS%5BAuthor%5D&cauthor=true&cauthor_uid=29794291

BACKGROUND AND AIMS: Provoked vestibulodynia (PVD) represent a longstanding pain syndrome that affects large numbers of women worldwide. However, no standardized guidelines for PVD treatment exist. In a cross-sectional pilot study we examined 30 PVD patients on multidimensional parameters including pain, psychological distress and quality of movement, in order to obtain a broader understanding of the somatic and psychological symptoms in PVD, and for the future to develop better interventions. Additionally, we compare the findings to previously published results regarding the same parameters in women with chronic pelvic pain (CPP). **METHODS:** Thirty women with PVD recruited from a tertiary care university clinic of gynecology were assessed for demographic data, pain intensity (VAS), psychological distress (GHQ-30 and Tampa scale of Kinesiophobia) and quality of movement (standardized Mensendieck test, SMT). **RESULTS:** Average age of the PVD women was 24.7±3.60 years, 60% of them were in permanent relationships, all were nulliparous, none had been subjected to surgical procedures, 100% were working full or part time and 90% were educated to at least undergraduate level. Mean VAS score was 7.77±1.97 (mean±SD), kinesiophobia 24.4±3.95 and anxiety domain of GHQ-30 9.73±4.06. SMT scores were particularly low for the domains of respiration and gait (less than 50% of optimal scores). **CONCLUSIONS:** PVD women display reduced quality of movement, especially for gait and respiration patterns, increased level of anxiety and high average pain scores.

These findings are similar to what we have previously reported in CPP patients. However, in contrast to CPP group, PVD women are on average younger, have higher work participation, higher education level and have not been subjected to surgical procedures. **IMPLICATIONS:** Since PVD women display similar, although somewhat less severe, symptom profile than CPP, we suggest that a multidimensional approach to treatment, such as "somatocognitive therapy" should be investigated in this group as it has previously been shown to be promising in treatment of CPP.

Co-morbid Disorders

An Online Cross-Sectional Comparison of Women With Symptoms of Persistent Genital Arousal, Painful Persistent Genital Arousal, and Chronic Vulvar Pain.

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

J Sex Med. 2018 Apr;15(4):558-567. doi: 10.1016/j.jsxm.2018.02.007.

<https://www.ncbi.nlm.nih.gov/pubmed/29609914>

BACKGROUND: Persistent genital arousal disorder (PGAD) is an understudied condition characterized by unwanted physiologic genital arousal in the absence of subjective sexual arousal. Markos and Dinsmore (*Int J STD AIDS* 2013;24:852-858) theorized that PGAD shares a number of similarities with vulvodynia (unexplained chronic vulvar pain [CVP]), including symptom characteristics and comorbidities. **AIM:** To compare medical histories, symptom characteristics, pain characteristics, and daily functioning among women with persistent genital pain (PGA) (n = 42), painful PGA (n = 37), and CVP (n = 42) symptoms. **METHODS:** An online cross-sectional survey was conducted from October 2015 through April 2016. **OUTCOMES:** Self-report measures of symptoms, diagnosed medical conditions, pain characteristics (McGill Pain Questionnaire), catastrophizing (Pain Catastrophizing Scale), and daily functioning (Functional Status Questionnaire) were collected. **RESULTS:** All 3 groups reported similar medical diagnoses and high frequencies of other chronic pelvic pain conditions. Women in all 3 groups reported comparable ages at symptom onset and timing of symptom expression (ie, constant vs intermittent). Women in the 2 PGA groups reported significantly greater feelings of helplessness than women in the CVP group. Women in the painful PGA and CVP groups endorsed significantly more sensory terms to describe their symptoms compared with women in the PGA group, whereas women in the painful PGA group reported significantly more affective terms to describe their symptoms compared with women in the CVP group. Women in the 2 PGA groups reported that their symptoms interfered significantly with most areas of daily functioning. **CLINICAL IMPLICATIONS:** Given the similarities between PGA and CVP symptoms, women with PGA may benefit from similar assessment, treatment, and research approaches. **STRENGTHS AND LIMITATIONS:** Limitations of the present study include its sole use of self-report measures; the presence of PGA or CVP symptoms was not confirmed by clinical assessment. However, the anonymous design of the online survey could have resulted in a larger and more diverse sample. **CONCLUSION:** The results of this study provide some initial support for the conceptualization of persistent genital arousal as a subtype of genital paresthesias/discomfort. These results also further highlight the negative impact that PGA symptoms have on many domains of daily living and the need for further research on this distressing condition. Jackowich RA, Pink L, Gordon A, et al. An Online Cross-Sectional Comparison of Women With Symptoms of Persistent Genital Arousal, Painful Persistent Genital Arousal, and Chronic Vulvar Pain.

Therapeutic Approaches of Botulinum Toxin in Gynecology.

Moga MA, Dimienescu OG, Bălan A, Scârneciu I, Barabaş B, Pleş L.

Toxins (Basel). 2018 Apr 21;10(4). pii: E169. doi: 10.3390/toxins10040169.

<https://www.ncbi.nlm.nih.gov/pubmed/29690530>

Botulinum toxins (BoNTs) are produced by several anaerobic species of the genus *Clostridium* and, although they were originally considered lethal toxins, today they find their usefulness in the treatment of a wide range of pathologies in various medical specialties. Botulinum neurotoxin has been identified in seven different isoforms (BoNT-A, BoNT-B, BoNT-C, BoNT-D, BoNT-E, BoNT-F, and BoNT-G). Neurotoxic Clostridia can produce more than 40 different BoNT subtypes and, recently, a new BoNT serotype (BoNT-X) has been reported in some studies. BoNT-X has not been shown to actually be an active neurotoxin despite its catalytically active LC, so it should be described as a putative eighth serotype. The mechanism of action of the serotypes is similar: they inhibit the release of acetylcholine from the nerve endings but their therapeutically potency varies. Botulinum toxin type A (BoNT-A) is the most studied serotype for therapeutic purposes. Regarding the gynecological pathology, a series of studies based on the efficiency of its use in the treatment of refractory myofascial pelvic pain, vaginism, dyspareunia, vulvodynia and overactive bladder or urinary incontinence have been reported. The current study is a review of the literature regarding the efficiency of BoNT-A in the gynecological pathology and on the long and short-term effects of its administration.

Physiotherapy for pelvic pain and female sexual dysfunction: an untapped resource.

Berghmans B.

Int Urogynecol J. 2018 May;29(5):631-638. doi: 10.1007/s00192-017-3536-8. Epub 2018 Jan 9.

<https://www.ncbi.nlm.nih.gov/pubmed/29318334>

INTRODUCTION AND HYPOTHESIS: Chronic pelvic pain (CPP) in women is a complex syndrome. Pain sensation and intensity often do not correspond with the identified lesion location but are felt elsewhere, leading to musculoskeletal and myofascial disorders and sexual dysfunction (SD). Although physical aspects are prevalent, they are often underdiagnosed and undertreated due to lack of understanding regarding its origin and distribution. Frequently, patients experience pelvic pain as psychological distress resulting in physical complaints, leading clinicians to prescribe medication or surgical intervention to correct or alleviate these symptoms, often with insufficient results. Because pelvic floor muscle disorders contribute significantly to CPP and SD, there is rationale for physiotherapy. However, physiotherapy is a widely underused and untapped resource, which has its place in the multidisciplinary approach to these health problems. **METHODS:** Computer-aided and manual searches and methodological quality assessment were carried out for meta-analyses, systematic reviews, and randomized controlled trials (RCTs) published between 1990 and 2017 investigating classification, assessment, and (physiotherapeutic) treatment of pelvic pain and/or female SD defined by the keywords below. Expert opinions were sought via interviews. **RESULTS:** Due to a lack of sufficient relevant medical information, referral data, and test results, focused physiotherapy is difficult to administer adequately. However, recent quality studies indicate significant clinical effects of physiotherapy for CPP and female SD, and experts advocate a multidisciplinary approach that includes physiotherapy. **CONCLUSIONS:** Because of its holistic approach, physiotherapy can contribute significantly to the multidisciplinary assessment and treatment of CPP and female SD.

Pudendal Neuralgia

Efficacy of Pulsed Radiofrequency Stimulation in Patients with Peripheral Neuropathic Pain: A Narrative Review.

Chang MC.

Pain Physician. 2018 May;21(3):E225-E234.

<https://www.ncbi.nlm.nih.gov/pubmed/29871378>

BACKGROUND: Recently, clinicians have been applying pulsed radiofrequency (PRF) stimulation on various peripheral nerves to manage patients' peripheral neuropathic pain. **OBJECTIVES:** To review the literature on the use and efficacy of PRF for controlling peripheral neuropathic pain. **STUDY DESIGN:** This is a narrative review of relevant articles on the effectiveness of PRF for peripheral neuropathic pain. **METHODS:** A PubMed search was conducted for papers published from January 1, 1980 to August 31, 2017 that used PRF to treat peripheral neuropathic pain. The key search phrase for identifying potentially relevant articles was [PRF AND pain]. The following inclusion criteria were applied for the selection of articles: 1) patients' pain was caused by peripheral nervous system disorders; 2) PRF stimulation was applied on the peripheral nerve; and 3) after PRF stimulation, follow-up evaluation was performed to assess the reduction in pain. Review articles were excluded. **RESULTS:** A total of 468 articles were found to be potentially relevant. After reading the titles and abstracts of the papers and assessing them for eligibility based on the full-text articles, 63 publications were finally included in this review. For radicular pain from spinal diseases, the evidence supports that PRF is an effective treatment. Similarly, PRF appears to be effective for postherpetic neuralgia and occipital neuralgia. On the other hand, for trigeminal neuralgia, the results of previous studies indicate that PRF is not appropriate for managing trigeminal neuralgia and less effective than conventional RF. However, data on the use of PRF for pudendal neuralgia, meralgia paresthetica, carpal tunnel syndrome, tarsal tunnel syndrome, and Morton's neuroma, is lacking and thus the efficacy of PRF in these peripheral nerve disorders cannot be determined at this time. **LIMITATIONS:** This review did not include studies indexed in databases other than PubMed. **CONCLUSIONS:** This review will help guide clinicians in making informed decisions regarding whether PRF is the appropriate option for managing the various peripheral neuropathic pain conditions in their patients.

Dermatological Conditions

Platelet-rich plasma (PRP) for the treatment of vulvar lichen sclerosus in a premenopausal woman: A case report.

Franić D, Iternička Z, Franić-Ivanišević M.

Case Rep Womens Health. 2018 Apr 16;18:e00062. doi: 10.1016/j.crwh.2018.e00062. eCollection 2018 Apr.

<https://www.ncbi.nlm.nih.gov/pubmed/29785390>

The use of platelet-rich plasma (PRP) for the treatment of lichen sclerosus (LS) in a 38-year-old premenopausal woman is reported. The diagnosis was confirmed histologically and the symptoms documented using the ICIQ Vaginal Symptoms Questionnaire (ICIQ-VS) and the Female Sexual Function Index (FSFI) questionnaire. PRP was prepared from autologous blood using the Regen Cellular Matrix Kit. PRP was administered twice over two months. Histology at follow-up one month after the second

administration showed the epidermis was nearly normal and upper dermal cellularity had been restored. The patient was symptom-free and both her ICIQ-VS and her FSFI scores had improved significantly. PRP is a potential new treatment option for LS which needs further assessment in randomized controlled trials.

Eosinophilic fasciitis and lichen sclerosus in a patient treated with nivolumab.

Andrés-Lencina JJ, Burillo-Martínez S, Aragón-Miguel R, Calleja-Algarra A, Rodríguez-Peralto JL, Ortiz-Romero PL, Gargallo-Moneva V.

Australas J Dermatol. 2018 May 24. doi: 10.1111/ajd.12836.

<https://www.ncbi.nlm.nih.gov/pubmed/29797309>

Skin and mucous membranes' manifestations of dermatological diseases within the genital area in females.

Plagens-Rotman K, Przybylska R, Adamski Z, Czarnecka-Operacz M.

Postepy Dermatol Alergol. 2018 Apr;35(2):199-203. doi: 10.5114/ada.2018.75243. Epub 2018 Apr 24.

<https://www.ncbi.nlm.nih.gov/pubmed/29760622>

Introduction: *Lichen sclerosus et atrophicus* (LSA) and an inversed type of psoriasis belong to a group of benign dermatoses usually located within the region of female external genitalia. The most common subjective symptoms reported by patients are itching, pain and changes in the color and structure of the skin. **Aim:** This paper presents 3 cases of patients suffering from selected dermatoses located within the external female genitalia treated at the Department of Dermatology, Poznan University of Medical Sciences. **Case reports:** Case 1. A 78-year-old patient admitted to the Department of Dermatology diagnosed with *lichen sclerosus and atrophic* as well as scleroderma, which had already been confirmed by histopathological examination in 2014. Laboratory tests demonstrated an increased level of glycemia, elevated ESR and lymphopenia. In the treatment of TFX (Thymus factor X) therapy (immunomodulating treatment), vitamins A + E containing cream and Protopic 0.1% ointment twice daily were recommended. Case 2. A patient aged 49 was admitted to the Department of Dermatology due to exacerbation of skin inflammation in the course of psoriasis. She presented with severe erythematous and papular lesions covered with silvery scales, with the highest intensity within the palmar surfaces of both hands, in the folds of under the breasts, groins, and therefore, the clinical picture was characteristic of inversed psoriasis (*psoriasis inversa*). Case 3. A 20-year-old patient admitted to the Department of Dermatology in order to proceed with the treatment of a diffuse type of scleroderma. Clinical diagnosis has been already confirmed by the skin biopsy (typical histological features of scleroderma), however exclusion of other dermatoses such as LSA was not possible.

Conclusions: While analyzing the available scientific reports, the physician in charge must adjust therapeutic options individually, taking into account the clinical condition of the patient in case of dermatological diseases within the female genital region.