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Vulvodynia

The Clinical Utility of the Vulvar Pain Assessment Questionnaire: A Pilot Study.

Dargie E, Pukall CF, Goetsch M, Stenson A, Leclair C.

J Low Genit Tract Dis. 2019 Oct;23(4):272-278. doi: 10.1097/LGT.0000000000000488.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=The+Clinical+Utility+of+the+Vulvar+Pain+Assessment+Questionnaire%3A+A+Pilot+Study>.

OBJECTIVE: The aim of the study was to document treatment-seeking experiences of women with chronic vulvar pain, comfort communicating about pain, and test the clinical utility of the screening version of the Vulvar Pain Assessment Questionnaire, screening version (VPAQscreen). **MATERIALS AND METHODS:** Patients scheduled for an appointment with the Program in Vulvar Health at Oregon Health and Science University were invited to complete the VPAQscreen and answer descriptive questions about previous treatment-seeking experiences and communication with health care providers. Clinicians provided provisional diagnoses based on VPAQscreen summaries, final diagnoses based on gynecological examination, and commented on alignment with clinical observations. Patients gave feedback on the accuracy and helpfulness of the VPAQscreen summary, characteristics of the questions asked, and whether their comfort communicating increased. **RESULTS:** Participants reported previously seeing approximately 5 medical doctors and 2 other health care providers and perceived them as lacking knowledge of vulvar pain syndromes. Providers indicated that VPAQscreen summaries aligned with clinical presentations and suggested provisional diagnoses with more than 80% accuracy. Participants reported that VPAQscreen summaries were helpful and accurate in summarizing symptoms. Most reported that the number, range, and readability of VPAQscreen questions were good or excellent. More than half reported that completing the VPAQscreen increased comfort when speaking with their Oregon Health and Science University physician. **CONCLUSIONS:** Patients with vulvar pain often endure a lengthy process of consulting multiple clinicians before securing care.

The VPAQscreen was more than 80% accurate in predicting diagnosis at this specialty clinic and was useful in assisting patients with expressing symptoms. The applicability of the VPAQscreen in general practice is unknown, although it shows promise.

Repeated Vaginal Exposures to the Common Cosmetic and Household Preservative Methylisothiazolinone Induce Persistent, Mast Cell-Dependent Genital Pain in ND4 Mice.

Arriaga-Gomez E, Kline J, Emanuel E, Neamonitaki N, Yangdon T, Zacheis H, Pasha D, Lim J, Bush S, Boo B, Mengistu H, Kinnamon R, Shields-Cutler R, Wattenberg E, Chatterjea D.

Int J Mol Sci. 2019 Oct 28;20(21). pii: E5361. doi: 10.3390/ijms20215361.

<https://www.ncbi.nlm.nih.gov/pubmed/31661848>

A history of allergies doubles the risk of vulvodynia—a chronic pain condition of unknown etiology often accompanied by increases in numbers of vulvar mast cells. We previously established the biological plausibility of this relationship in mouse models where repeated exposures to the allergens oxazolone or dinitrofluorobenzene on the labial skin or inside the vaginal canal of ND4 Swiss Webster outbred mice led to persistent tactile sensitivity and local increases in mast cells. In these models, depletion of mast cells alleviated pain. While exposure to cleaning chemicals has been connected to elevated vulvodynia risk, no single agent has been linked to adverse outcomes. We sensitized female mice to methylisothiazolinone (MI)—a biocide preservative ubiquitous in cosmetics and cleaners—dissolved in saline on their flanks, and subsequently challenged them with MI or saline for ten consecutive days in the vaginal canal. MI-challenged mice developed persistent tactile sensitivity, increased vaginal mast cells and eosinophils, and had higher serum Immunoglobulin E. Therapeutic and preventive intra-vaginal administration of Δ^9 -tetrahydrocannabinol reduced mast cell accumulation and tactile sensitivity. MI is known to cause skin and airway irritation in humans, and here we provide the first pre-clinical evidence that repeated MI exposures can also provoke allergy-driven genital pain.

Pain, Anxiety, Depression, and Quality of Life in Patients with Vulvodynia.

Tribó MJ, Canal C, Baños JE, Robleda G

Dermatology. 2019 Nov 6:1-7. doi: 10.1159/000503321.

<https://www.ncbi.nlm.nih.gov/pubmed/31694025>

BACKGROUND/AIMS: The term vulvodynia refers to vulvar pain of unknown origin lasting at least 3 months. Psychiatric comorbidities are a common feature and, along with pain, may severely affect patients' wellbeing. We aimed to determine the characteristics of pain in vulvodynia, to correlate characteristics with symptoms of anxiety and depression, and to analyse the impact of these factors on patients' quality of life. **METHODS:** This cross-sectional observational study analysed pain, anxiety, and depression and the effects of these factors on quality of life. Pain, anxiety, and depression were assessed using validated tools in 110 women. **RESULTS:** Statistical analyses found correlations between pain and anxiety and between anxiety and worsened quality of life. Patients often reported stinging, burning, pain, itching, and dyspareunia, pointing to the importance of temporal, localisation, punctate pressure, thermal, tactile sensitivity, and emotional tension characteristics. Most patients had severe pain related to psychiatric comorbidities and decreased quality of life. **CONCLUSION:** Using descriptors of pain quality and assessing anxiety and depression might help to define subgroups of patients that may benefit from different therapeutic approaches and thus enable treatments to be tailored to individual patients.

Acupuncture Augmentation of Lidocaine for Provoked, Localized Vulvodynia: A Feasibility and Acceptability Study.

Hullender Rubin LE, Mist SD, Schnyer RN, Chao MT, Leclair CM.

J Low Genit Tract Dis. 2019 Oct;23(4):279-286. doi: 10.1097/LGT.0000000000000489.

<https://www.ncbi.nlm.nih.gov/pubmed/31592976>

OBJECTIVE: The aim of the study was to assess the feasibility and acceptability of acupuncture's augmentation of lidocaine therapy in the treatment of provoked localized vulvodynia (PLV).

MATERIALS AND METHODS: For 12 weeks, women with moderate to severe PLV were randomized to either 18 sessions of traditional acupuncture (TA) or non-TA (NTA). All participants applied lidocaine 5% cream 4 times daily to the vestibule. Feasibility was assessed by recruitment, enrollment, assessment completion, and blinding. Acceptability was assessed by study visit attendance and satisfaction. The primary outcome was change in tampon test scores from baseline to week 12 and follow-up at week 24. **RESULTS:** Nineteen women enrolled and 14 completed the study. Five withdrew because of lidocaine reaction (n = 2), inability to insert tampon (n = 1), starting a new medication (n = 1), or change in vulvar diagnosis (n = 1). Participants in both groups reported pain reduction for 12 weeks. There was no statistically significant difference between groups. Women in the TA group (n = 7) experienced less pain from baseline to 12 weeks (mean difference [MD] = 42.4 ± 19.4 and MD = 35.7 ± 17.8 at week 24). In the non-TA group (n = 7), women experienced a within-group MD of 28.7 ± 28.5 at 12 weeks and an MD of 36.7 ± 17.7. **CONCLUSIONS:** In this early-phase research, acupuncture augmentation of lidocaine was acceptable. The study procedures, with modifications, may be feasible for future investigation. Both acupuncture techniques showed a favorable effect; however, the contribution to pain relief is undetermined.

Spiroglactone May be a Cause of Hormonally Associated Vestibulodynia and Female Sexual Arousal Disorder.

Mitchell L, Govind V, Barela K, Goldstein AT.

J Sex Med. 2019 Sep;16(9):1481-1483. doi: 10.1016/j.jsxm.2019.06.012. Epub 2019 Jul 24.

<https://www.ncbi.nlm.nih.gov/pubmed/31351850>

BACKGROUND: Although spiroglactone is an effective treatment for androgen-mediated cutaneous disorders, the potential sexual side-effects are poorly documented in current literature. **AIM:** The purpose of this study was to provide clinical evidence that spiroglactone may be a cause of hormonally associated vestibulodynia and female sexual arousal disorder. **METHODS:** A database search of a vulvar disorders clinic revealed 7 cases in which spiroglactone may have caused or contributed to dyspareunia and decreased arousal. In all cases, the patients stopped taking spiroglactone and used a compounded estradiol 0.01%/testosterone 0.1% gel to the vestibule twice daily. 2 cases are discussed to further illustrate these previously unreported side effects. **OUTCOMES:** Improvement in sexual function was determined after treatment. **RESULTS:** Examination of women taking spiroglactone who presented with the complaints of introital dyspareunia revealed vulvar vestibular atrophy and tenderness, especially at the glandular ostia. After stopping spiroglactone and applying a topical estrogen/testosterone gel to the vestibule, all women had significant improvement in their vulvar atrophy, resolution of their dyspareunia, and improved sexual arousal.

CLINICAL IMPLICATIONS: Use of spironolactone may be a cause of hormonally associated vestibulodynia and female sexual arousal disorder. **STRENGTHS AND LIMITATIONS:** The influence of spironolactone on vulvar health and sexual function is poorly documented in the medical literature. The strength of this paper is that it examines the potential deleterious side effects of this medication on female sexual function. However, the most significant limitation of this case series is that it was not a prospective, controlled study. **CONCLUSIONS:** Although treatment of androgen-mediated cutaneous disorders is warranted, medical providers should be aware of the potential sexual side effects of this anti-androgenic medication. Mitchell L, Govind V, Barela K, et al. Spironolactone May be a Cause of Hormonally Associated Vestibulodynia and Female Sexual Arousal Disorder.

Self-Efficacy Mediates the Attachment-Pain Association in Couples with Provoked Vestibulodynia: A Prospective Study.

Charbonneau-Lefebvre V, Vaillancourt-Morel MP, Brassard A, Steben M, Bergeron S.

J Sex Med. 2019 Nov;16(11):1803-1813. doi: 10.1016/j.jsxm.2019.08.012. Epub 2019 Sep 26.

<https://www.ncbi.nlm.nih.gov/pubmed/31564535>

INTRODUCTION: Attachment influences the way individuals anticipate, react, and seek support when faced with chronic pain. Although cross-sectional research indicates that attachment insecurity and pain self-efficacy are associated with pain intensity in chronic pain populations, little is known about their long-term effects on pain, and about the directionality of associations between these constructs. Furthermore, whereas attachment is a relational concept, few studies on genito-pelvic pain have espoused a couples' perspective. **AIM:** Using a prospective dyadic design, the present study aimed to examine the directionality of the associations among attachment dimensions, pain self-efficacy, and pain intensity in couples coping with provoked vestibulodynia (PVD). A second aim was to test whether pain self-efficacy mediated the attachment-pain association. **METHODS:** 213 couples coping with PVD completed self-report questionnaires at baseline (T1) and at a 2-year follow-up (T2). **MAIN OUTCOME MEASURE:** (1) Experiences in Close Relationships - Revised; (2) Painful Intercourse Self-Efficacy Scale; and (3) 10-point Numerical Rating Scale for pain intensity. **RESULTS:** Autoregressive cross-lagged models revealed that women's greater attachment anxiety and avoidance at T1 predicted their greater pain intensity at T2. Women's greater attachment anxiety at T1 predicted their poorer pain self-efficacy at T2, and poorer pain self-efficacy in women at T1 predicted their higher pain intensity at T2. A mediation model showed that women's lower pain self-efficacy at T2 fully mediated the association between women's higher attachment anxiety at T1 and their higher pain intensity at T2. Partners' attachment dimensions did not predict their own or women's pain self-efficacy nor pain intensity. **CLINICAL IMPLICATIONS:** Results suggest that greater attachment anxiety may contribute to women with PVD's lower confidence that they can manage their pain, which leads to long-term persistent pain. This study highlights the importance of assessing attachment and pain self-efficacy in women with genito-pelvic pain and to consider interventions targeting these variables, as they have far-reaching consequences. **STRENGTH & LIMITATIONS:** The use of longitudinal and dyadic data inform interpersonal processes and the long-term implications of attachment and pain self-efficacy in PVD. The use of self-report measures may introduce a social desirability and recall bias. **CONCLUSION:** This prospective dyadic study adds to a body of literature on PVD and chronic pain by empirically supporting theoretical models on attachment, pain self-efficacy, and persistent pain, and supports the role of psychosocial factors in the adjustment to PVD. Charbonneau-Lefebvre V, Vaillancourt-Morel M-P, Brassard A, et al. Self-Efficacy Mediates the Attachment-Pain Association in Couples with Provoked Vestibulodynia: A Prospective Study.

The association of vulvar pain and urological urgency and frequency: findings from a community-based case-control study.

Sun Y, Harlow BL.

Int Urogynecol J. 2019 Nov;30(11):1871-1878. doi: 10.1007/s00192-019-04052-2. Epub 2019 Aug 2. <https://www.ncbi.nlm.nih.gov/pubmed/31375872>

INTRODUCTION AND HYPOTHESIS: Vulvodynia is chronic debilitating burning vulvar pain or pain on contact. Although women who suffer from vulvodynia are more likely than others to experience co-morbid interstitial cystitis (IC) and urinary tract infections (UTIs), few studies have explored whether women with vulvodynia experience adverse urinary symptoms (lower urinary tract symptoms [LUTS]) in the absence of urological pain. **METHODS:** Two hundred and eleven participants with and 226 participants without clinically confirmed vulvodynia completed the Pelvic Pain and Urgency/Frequency (PUF) questionnaire and were scored using all questions, and then a subset of questions relating only to their current frequency and bother of urination during day and night, and the frequency, severity and bother of urgency after voiding. Total, symptom, and bother scores were compared in women with and without vulvodynia, and regression models estimated adjusted odds ratios and 95% confidence intervals for the various LUTS symptoms. **RESULTS:** As expected, 40% of women with vulvodynia met the criteria for IC (PUF > 12) compared with 2% without vulvodynia. After excluding questions related to bladder or vulvovaginal pain, women with vulvodynia, compared with those without, were skewed toward higher PUF scores, including being 2.4 times more likely to report usually or always bothered by night-time voiding (95% CI 1.22-4.74), and 18 times more likely to report moderate/severe urgency after urination (95% CI 5.48-64.12). **CONCLUSIONS:** Women with vulvodynia are substantially more likely to report voiding dysfunction and symptoms of urgency than women with no history of vulvar pain. These findings are independent of comorbid interstitial cystitis or history of UTIs.

Injectable Botulinum Toxin for Pelvic Pain: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines [Internet].

Wells C, Farrah K.

Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Aug.

CADTH Rapid Response Reports.

<https://www.ncbi.nlm.nih.gov/pubmed/31697458>

Gynecological conditions of the pelvic floor region can include vulvodynia (vulvar pain lasting at least 3 months with no identifiable cause),¹ vaginismus (or genito-pelvic pain or penetration disorder, the inability to achieve non-painful vaginal penetration of any kind),² endometriosis (in which cells of the endometrium grows outside of the uterus), and provoked vestibulodynia (localized pain in the vulvar vestibule caused by physical contact).³ Gynecological conditions of the pelvic floor region are generally considered to occur as a result of a multifactorial process that includes genetics, hormonal changes, inflammation, musculoskeletal issues (such as hypertonic muscles), neurologic mechanisms, psychosocial factors (often related to sexual functioning), and structural issues (such as perineal descent), but etiologies are often unknown.^{1,4,5} First-line treatments for these conditions include physiotherapy, dilation therapy, sex counseling, psychotherapy, or a combination of therapies.^{2,6} Increasingly, botulinum toxin has become an alternative therapy option for individuals with pelvic pain.⁶ Botulinum toxin is a toxin produced by the *Clostridium* bacteria.⁶ Botulinum toxin is used in

neuromuscular disorders, ophthalmic disorders, chronic pain, cosmetic and dermatological applications, pelvic floor disorders, gastrointestinal disorders, and spasticity.⁶ In pelvic pain, it is typically injected into the muscle, where it inhibits release of acetylcholine, causing blockage of muscle spasms.⁶ Pelvic pain disorders can affect an individual's feelings of self worth, quality of life, sexual functioning, psychological well being, and relationships.¹⁻³ According to a 2017 cross-sectional study, the average hospital-associated cost of chronic pelvic pain (pelvic and perineal pain, dysmenorrhea, or dyspareunia) in Canada amounted to C\$25 million per year between 2008 and 2012.⁷ Many cases of pelvic pain go undiagnosed, as patients often do not report sexual dysfunction, and it has been reported that patients with vulvodynia had the condition for an average of 7 years before seeking help.^{2,3} Additionally, as vulvodynia is not well understood, individuals with the condition may wait an average of 5 years to receive a diagnosis after seeking treatment.³ There is uncertainty regarding the effectiveness of botulinum toxin for some chronic pelvic pain conditions. The purpose of this report is to evaluate the evidence regarding the clinical effectiveness and safety of botulinum toxin compared with other treatments or placebo for patients with chronic pelvic floor dysfunction and pain. Evidence regarding the cost-effectiveness of botulinum toxin for pelvic pain was also sought to support decision making. Evidence-based recommendations were sought to provide guidance on the use of botulinum toxin for these conditions.

Pelvic floor physical therapy in the treatment of pelvic floor dysfunction in women.

Wallace SL, Miller LD, Mishra K.

Curr Opin Obstet Gynecol. 2019 Dec;31(6):485-493. doi: 10.1097/GCO.0000000000000584.

<https://www.ncbi.nlm.nih.gov/pubmed/31609735>

PURPOSE OF REVIEW: To describe the principles of pelvic floor physical therapy (PFPT), review the evidence for PFPT as a treatment for pelvic floor dysfunction, and summarize the current recommendations for PFPT as a first-line conservative treatment option for pelvic floor disorders.

RECENT FINDINGS: Pelvic floor dysfunction can cause voiding and defecation problems, pelvic organ prolapse (POP), sexual dysfunction, and pelvic pain. PFPT is a program of functional retraining to improve pelvic floor muscle strength, endurance, power, and relaxation in patients with pelvic floor dysfunction. Based on the available evidence, PFPT with or without supplemental modalities can improve or cure symptoms of urinary incontinence, POP, fecal incontinence, peripartum and postpartum pelvic floor dysfunction, and hypertonic pelvic floor disorders, including pelvic floor myofascial pain, dyspareunia, vaginismus, and vulvodynia. Currently, there is conflicting evidence regarding the effectiveness of perioperative PFPT before or after POP and urinary incontinence surgery.

SUMMARY: PFPT has robust evidence-based support and clear benefit as a first-line treatment for most pelvic floor disorders. Standards of PFPT treatment protocols, however, vary widely and larger well designed trials are recommended to show long-term effectiveness.

Persistent Genital Arousal Disorder: Review of Pertinent Peripheral Nerves.

Klifton KM, Dellon AL.

Sex Med Rev. 2019 Nov 5. pii: S2050-0521(19)30100-3. doi: 10.1016/j.sxmr.2019.10.001.

<https://www.ncbi.nlm.nih.gov/pubmed/31704111>

INTRODUCTION: Persistent genital arousal disorder (PGAD) is a condition that is still poorly understood. Etiologies reported for PGAD are vascular, neurological, pharmacological, and psychological. Determining the neurophysiological etiology of PGAD began with developing an understanding of the

underlying biomechanics of the pudendal nerve and the female sexual response. **AIM:** To summarize the anatomy, physiology, etiologies, diagnostics, and treatments of the pertinent peripheral nerves involved in the pathology of PGAD. **METHODS:** We performed a PubMed, Cochrane, Embase, Web of Science, and Google Scholar search for English-language articles in peer-reviewed journals with no predefined time period for inclusion. Terms included "humans"[All Fields] AND "persistent"[All Fields] AND/OR ("genitalia"[All Fields] OR "genital"[All Fields]) AND/OR "arousal"[All Fields] AND/OR ("disease"[All Fields] OR "disorder"[All Fields]) AND/OR "nerve"[All Fields]. The main outcomes of the papers were reviewed. **MAIN OUTCOME MEASURE:** The main outcome measures were the anatomy and physiology, etiologies, history and physical examination, diagnostic imaging, and current evidence for the treatment of PGAD related to the peripheral nervous system. **RESULTS:** Most of the literature for PGAD originates from case studies. The diagnosis of PGAD itself is still a debated topic of discussion. More recent data published indicate that this disease affects males, as well. **CONCLUSION:** Nerve entrapment may be a source of continuous arousal. Associated PGAD symptoms would depend on the segment of the nerve involved. Unwelcomed or unwanted arousal has been observed as the most common detrimental symptom. Pelvic 3-tesla magnetic resonance imaging is recommended in all patients with suspected nerve entrapment. Lumbosacral 3-tesla magnetic resonance imaging is recommended if a Tarlov cyst or a herniated intervertebral disc is suspected. If the peripheral nerve is the source of the pathology, surgical intervention may be curative. A multidisciplinary team approach consisting of a medical provider, pelvic floor physical therapist, and sex therapist has demonstrated benefits. There are currently no Food and Drug Administration-approved evidenced-based treatments for PGAD. Klifto KM, Dellon AL. Persistent Genital Arousal Disorder: Review of Pertinent Peripheral Nerves.

Benefits and Harms of Electrical Neuromodulation for Chronic Pelvic Pain: A Systematic Review.

Cottrell AM, Schneider MP, Goonewardene S, Yuan Y, Baranowski AP, Engeler DS, Borovicka J, Dinis-Oliveira P, Elneil S, Hughes J, Messelink BJ, de C Williams AC.

Eur Urol Focus. 2019 Oct 19. pii: S2405-4569(19)30287-1. doi: 10.1016/j.euf.2019.09.011

<https://www.ncbi.nlm.nih.gov/pubmed/31636030>

CONTEXT: Patients with chronic pelvic pain (CPP) may have pain refractory to conventional pain management strategies. Neuromodulation could provide relief of pain. **OBJECTIVE:** To evaluate the benefits and harms of neuromodulation for CPP. **EVIDENCE ACQUISITION:** A comprehensive search of EMBASE, PUBMED, and SCOPUS was performed for the entire database to January 2018. Studies were selected, data were extracted, and quality was assessed by two independent reviewers. A meta-analysis was used to combine randomized controlled trials (RCTs); otherwise, a narrative analysis was used. **EVIDENCE SYNTHESIS:** After screening 1311 abstracts, 36 studies including eight RCTs were identified, enrolling 1099 patients. Studies covered a broad range in terms of phenotypes of CPP and methods of neuromodulation. A meta-analysis was possible for percutaneous tibial nerve stimulation and transcutaneous electrical nerve stimulation, which showed improvement in pain. Only narrative synthesis was possible for other modalities (sacral nerve stimulation, spinal cord stimulation, intravaginal electrical stimulation, and pudendal nerve stimulation) which appeared to reduce pain in patients with CPP. Treatments generally improved quality of life but with variable reporting of adverse events. Many studies showed high risks of bias and confounding. **CONCLUSIONS:** While electrical neuromodulation may improve symptoms in CPP, further work is needed with high-quality studies to confirm it. **PATIENT SUMMARY:** Neuromodulation may be useful in reducing pain and improving quality of life in patients with chronic pelvic pain, but more research is needed.

Painful interactions: Microbial compounds and visceral pain.

van Thiel IAM, Botschuijver S, de Jonge WJ, Seppen J.

Biochim Biophys Acta Mol Basis Dis. 2019 Oct 18;165534. doi: 10.1016/j.bbadis.2019.165534.

<https://www.ncbi.nlm.nih.gov/pubmed/31634534>

Visceral pain, characterized by abdominal discomfort, originates from organs in the abdominal cavity and is a characteristic symptom in patients suffering from irritable bowel syndrome, vulvodynia or interstitial cystitis. Most organs in which visceral pain originates are in contact with the external milieu and continuously exposed to microbes. In order to maintain homeostasis and prevent infections, the immune- and nervous system in these organs cooperate to sense and eliminate (harmful) microbes. Recognition of microbial components or products by receptors expressed on cells from the immune and nervous system can activate immune responses but may also cause pain. We review the microbial compounds and their receptors that could be involved in visceral pain development.

Myofascial Release for Vulvar Pain and Pubic Shear After a Straddle Injury in a 3-Year-Old Girl.

Dade MM, Broecker JD.

J Am Osteopath Assoc. 2019 Nov 1;119(11):768-771. doi: 10.7556/jaoa.2019.127.

<https://www.ncbi.nlm.nih.gov/pubmed/31657831>

Pelvic malalignment is a somatic dysfunction that can lead to pelvic discomfort, despite normal genital examination findings. A 3-year-old girl presented with vulvar discomfort after a straddle injury sustained while riding a tricycle. The symptoms persisted despite standard medical treatment for vulvovaginitis and chronic vulvar irritation. An osteopathic structural examination revealed distortions of the bony pelvis, often associated with genitourinary complaints. After 5 osteopathic manipulative treatment sessions, the patient experienced significant relief. With persistent vulvar pain, somatic dysfunction should be considered in the differential diagnosis. A brief musculoskeletal examination of the pubic tubercles, iliac crest, and iliac spines can help to identify somatic dysfunction in a gynecologic patient with symptoms that are unresponsive to standard treatments.

Relationship Context Moderates Couple Congruence in Ratings of Sexual Arousal and Pain During Vaginal Sensations in the Laboratory.

Dewitte M, Schepers J.

Arch Sex Behav. 2019 Sep 3. doi: 10.1007/s10508-019-1452-3.

<https://www.ncbi.nlm.nih.gov/pubmed/31482424>

Genital pain is a social experience that needs to be studied as a dyadic interaction between partners. The present study relied on a sample of 42 heterosexual couples to examine the level of congruence between both partners' ratings of pain and sexual arousal in response to experimentally induced vaginal pressure that served as a simulation of vaginal sensations during penetration. We also inferred the men's ability to estimate their partner's level of pain and sexual arousal. Because the relationship has shown to influence pain estimations, we considered the moderating role of perceived partner responsiveness and relationship satisfaction. We found higher disagreement in pain ratings when vaginal pressure was induced in the context of a sexual film compared to a neutral film, with men overestimating the level of pain in women. Also sexual arousal ratings diverged between partners, with men underestimating their partners' level of sexual arousal during the induction of vaginal pressure, regardless of whether they were watching a sexual or neutral film. Importantly, the level of congruence

between actual and estimated ratings of pain and sexual arousal depended on how relationally satisfied men and women were and how validated and supported women felt by their male partner. These results make an important contribution to the growing literature on the social determinants of sexual pain experiences.

Pudendal Neuralgia

Role of 3 Tesla MR Neurography and CT-guided Injections for Pudendal Neuralgia: Analysis of Pain Response.

Ly J, Scott K, Xi Y, Ashikyan O, Chhabra A.

Pain Physician. 2019 Jul;22(4):E333-E344.

<https://www.ncbi.nlm.nih.gov/pubmed/31337177>

BACKGROUND: Magnetic resonance neurography (MRN) has an increasing role in the diagnosis and management of pudendal neuralgia, a neurogenic cause of chronic pelvic pain. **OBJECTIVE:** The objective of this research was to determine the role of MRN in predicting improved pain outcomes following computed tomography (CT)-guided perineural injections in patients with pudendal neuralgia. **STUDY DESIGN:** This study used a retrospective cross-sectional study design. **SETTING:** The research was conducted at a large academic hospital. **METHODS:** Patients: Ninety-one patients (139 injections) who received MRN and CT-guided pudendal blocks were analyzed. **INTERVENTION:** A 3Tesla (T) scanner was used to evaluate the lumbosacral plexus for pudendal neuropathy. Prior to receiving a CT-guided pudendal perineural injection, patients were given pain logs and asked to record pain on a visual analog scale. **MEASUREMENT:** MRN findings for pudendal neuropathy were compared to the results of the CT-guided pudendal nerve blocks. Injection pain responses were categorized into 3 groups - positive block, possible positive block, and negative block. **Statistical Tests:** A chi-square test was used to test any association, and a Cochran-Armitage trend test was used to test any trend. Significance level was set at .05. All analyses were done in SAS Version 9.4 (SAS Institute, Inc., Cary, NC). **RESULTS:** Ninety-one patients (139 injections) who received MRN were analyzed. Of these 139 injections, 41 were considered positive (29.5%), 52 of 139 were possible positives (37.4%), and 46 of 139 were negative blocks (33.1%). Of the patients who had a positive pudendal block, no significant difference was found between the MRN result and the pudendal perineural injection response ($P = .57$). Women had better overall response to pudendal blocks, but this response was not associated with MRN findings ($P = .34$). However, positive MRN results were associated with better pain response in men ($P = .005$). Patients who reported bowel dysfunction also had a better response to pudendal perineural injection ($P = .02$). **LIMITATIONS:** Some limitations include subjectivity of pain reporting, reporting consistency, absence of a control group, and the retrospective nature of the chart review. **CONCLUSION:** Pudendal perineural injections improve pain in patients with pudendal neuralgia and positive MRN results are associated with better response in men.

Pudendal Nerve Entrapment Syndrome.

Kaur J, Singh P.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-.

2019 Jun 21.

<https://www.ncbi.nlm.nih.gov/pubmed/31334992>

Pudendal neuralgia caused by pudendal nerve entrapment (PNE) is a chronic and severely disabling neuropathic pain syndrome.[1] It presents in the pudendal nerve region and affects both males and females. It is mostly underdiagnosed and inappropriately treated, and causes significant impairment of quality of life. Anatomy of the Pudendal Nerve: The pudendal nerve emerges from the S2, S3, and S4 roots' ventral rami of the sacral plexus. It carries sensory, motor, and autonomic fibers, however an injury to the pudendal nerve causes sensory deficits more than motor. It courses between two muscles, piriformis and coccygeus muscles. It departs the pelvic cavity through the greater sciatic foramen ventral to the sacrotuberous ligament. At the ischial spine level, it passes medial to and under the sacrospinous ligament to re-enter the pelvic cavity through a lesser sciatic foramen. The pudendal nerve then courses in the pudendal canal, which is also called the Alcock canal. The three last branches of the pudendal nerve terminate in the ischioanal fossa. These are the inferior rectal branch, perineal branch, and dorsal sensory nerve of the penis or clitoris. However, there are case reports which have shown variability in the anatomy of the pudendal nerve.[2][3] Pudendal nerve compression based on anatomy[4][5]: The pudendal nerve entrapment syndromes subdivide into four types based on the level of compression. Type I - Entrapment below the piriformis muscle as the pudendal nerve exits greater sciatic notch. Type II - Entrapment between sacrospinous and sacrotuberous ligaments - this is the most common cause of nerve entrapment. Type III - Entrapment in the Alcock canal. Type IV - Entrapment of terminal branches.

Dermatological Conditions

Usefulness of video thermography in the evaluation of platelet-rich plasma effectiveness in vulvar lichen sclerosis: preliminary study.

Tedesco M, Garelli V, Elia F, Chicherchia G, Foddai ML, Latini A, Morrone A, Migliano E.

J Dermatolog Treat. 2019 Nov 7:1-4. doi: 10.1080/09546634.2019.1685644.

<https://www.ncbi.nlm.nih.gov/pubmed/31648588>

Background: Lichen sclerosis (LS) is a chronic-relapsing and potentially serious skin disease that has a preference for genital skin. Currently, there is no standardized method for assessing the effects of therapies. **Objective:** The objective of this preliminary study is to use video thermography (VTG) in the evaluation of vulvar lichen sclerosis (VLS) before and after platelet-rich plasma (PRP) therapy. **Methods:** A sample of six female patients was enrolled. Patients were subjected to PRP treatment. Patients selected for the study had been assessed at baseline (T0) and after 7 and 30 d from PRP treatment (T1 and T2, respectively). Clinical and VTG evaluation was executed in every visit. **Results:** The VTG examination showed at least one hypothermic area (HA) in all our patients. The average temperature measured in the vulvar and perineal region taken as a reference for each patient was found to be between 33.7 °C and 36.3 °C, with a fair difference between the patients. HAs showed thermal differences which varied between 2.2 °C and 1.2 °C. **Conclusions:** It is demonstrated here that PRP offers satisfactory effectiveness in treating VLS and that video thermography could represent a useful paraclinic method in the identification and follow-up of LS.

Evaluation of the efficacy of 5-aminolevulinic acid photodynamic therapy for the treatment of vulvar lichen sclerosis.

Li Z, Wang Y, Wang J, Li S, Xiao Z, Feng Y, Gu J, Li J, Peng X, Li C, Zeng K.

Photodiagnosis Photodyn Ther. 2019 Nov 5:101596. doi: 10.1016/j.pdpdt.2019.101596.

<https://www.ncbi.nlm.nih.gov/pubmed/31704505>

BACKGROUND: This study aimed to evaluate the effects of 5-aminolevulinic acid photodynamic therapy (ALA-PDT) on the improvement of symptoms and recurrence rate in patients with vulvar lichen sclerosis (VLS) and observe its side effects. **METHODS:** The symptom scores before and after photodynamic therapy (PDT) in 13 enrolled patients with VLS were analyzed retrospectively. All patients were followed-up for at least 6 months to evaluate the recurrence rate after PDT. The patients were treated with PDT only during the study period. During the PDT treatment, a 20% 5-aminolevulinic acid solution was applied to the lesions and marginal areas for 3 hours, and the entire area was then irradiated with 635 nm red light of 80 J/cm² at 80 mW/cm² for 30 minutes. **RESULTS:** In this study, the effective rate of PDT was 92.31%. Lesions recurred in two patients at 6 months after PDT. Post-treatment, the total subjective, total objective, and the Dermatological Life Quality Index scores changed from 11.4, 4.3, and 13.4 at baseline to 4.9, 2, and 5.9, respectively. The difference was statistically significant (p <0.05). PDT was mildly toxic in most patients. **CONCLUSIONS:** ALA-PDT is a safe and effective method for the treatment of VLS, and the therapeutic effects can be maintained for at least 3 months. The therapeutic effects may decrease during the 3-6-month period after PDT.

An arm-based network meta-analysis on treatments for vulvar lichen sclerosis and a call for development of core outcome sets: Treatment options for vulvar lichen sclerosis.

Pergialiotis V, Bellos I, Biliou EC, Varnava P, Mitsopoulou D, Doumouchtsis SK.

Am J Obstet Gynecol. 2019 Nov 4. pii: S0002-9378(19)31321-3. doi: 10.1016/j.ajog.2019.10.095.

<https://www.ncbi.nlm.nih.gov/pubmed/31697910>

OBJECTIVE: The purpose of the present systematic review is to evaluate the available medical treatments for vulvar lichen sclerosis, using an arm based network meta-analysis protocol. **DATA SOURCES:** We searched Medline (1966-2019), Scopus (2004-2019), Cochrane Central Register of Controlled Trials CENTRAL (1999-2019) and Clinicaltrials.gov (2008-2019) databases. Google Scholar (2004-2019) database, along with the reference list of all included studies. **STUDY ELIGIBILITY CRITERIA:** All observational, randomized and single arm studies that evaluated medical treatments for vulvar lichen sclerosis were considered eligible for inclusion in the present systematic review. **STUDY APPRAISAL:** Network meta-analysis was carried-out in R-3.4.3 using the "pcnetmeta" package which uses a Bayesian hierarchical model (based in Markov Chain Monte Carlo Convergence (MCMC) simulation). **RESULTS:** Sixteen studies were included in this present meta-analysis which recruited 954 women with vulvar lichen sclerosis. Their quality was evaluated with the JADAD, Cochrane risk of bias and ROBINS-I tools. Clobetasol treatment ranked as the best treatment for disease remission after evaluating rank probabilities [40% chance of ranking 1st compared to tacrolimus (38%)]. However, the density plot revealed partial overlapping with tacrolimus. The lowest probability of experiencing a relapse was observed with pimecrolimus (15% [2-48%]); however, the density plot revealed significant overlapping with mometasone furoate, testosterone and clobetasol. **CONCLUSION:** Robust evidence concerning the superiority of potent steroids at least over calcineurin inhibitors is still lacking in the field of vulvar lichen sclerosis. On the other hand, the gross heterogeneity in terms of selected population, duration of treatment, administered regimen, outcome reporting and selection of outcome measures leaves several fields unanswered.

Lichen Sclerosus: An autoimmunopathogenic and genomic enigma with emerging genetic and immune targets.

Tran DA, Tan X, Macri CJ, Goldstein AT, Fu SW.

Int J Biol Sci. 2019 Jun 2;15(7):1429-1439. doi: 10.7150/ijbs.34613. eCollection 2019.

<https://www.ncbi.nlm.nih.gov/pubmed/31337973>

Lichen sclerosus (LS) is an inflammatory dermatosis with a predilection for anogenital skin. Developing lesions lead to vulvar pain and sexual dysfunction, with a significant loss of structural anatomical architecture, sclerosis, and increased risk of malignancy. Onset may occur at any age in both sexes, but typically affects more females than males, presenting in a bimodal fashion among pre-pubertal children and middle-aged adults. A definitive cure remains elusive as the exact pathogenesis of LS remains unknown. A general review of LS, histologic challenges, along with amounting support for LS as an autoimmune disease with preference for a T_h1 immune response against a genetic background is summarized. In addition to the classically referenced ECM1 (extracellular matrix protein 1), a following discussion of other immune and genetic targets more recently implicated as causative or accelerant agents of disease, particularly miR-155, downstream targets of ECM1, galectin-7, p53, and epigenetic modifications to CDKN2A, are addressed from the viewpoint of their involvement in three different, but interconnected aspects of LS pathology. Collectively, these emerging targets serve not only as inherently potential therapeutic targets for treatment, but may also provide further insight into this debilitating and cryptic disease.

Oral and Vulvar Lichen Sclerosus.

Vučičević Boras V, Škrinjar I, Batelja Vuletić L, Bradamante M, Bartenjev I, Ljubojević Hadžavdić S.

Acta Dermatovenerol Croat. 2019 Sep;27(3):195-197.

<https://www.ncbi.nlm.nih.gov/pubmed/31542067>

Lichen sclerosus (LS) is a chronic, inflammatory, mucocutaneous disorder of genital and extragenital skin (1). Simultaneous involvement of the oral mucosa is extremely rare, but it may be the only affected area (2). A 55-year-old woman was referred to the Department of Oral Medicine, School of Dental Medicine University of Zagreb due to whitish lesions on the right ventrolateral part of the tongue and buccal mucosa with desquamative gingivitis (Figure 1, a-c). The lesions were asymptomatic but indurated on palpation. Histology was conclusive for oral lichen sclerosus (OLS). The lesions on gingiva were successfully treated with betamethasone ointment, three times a day for two weeks. One year earlier, she had been referred to the Department of Dermatology and Venereology with progressive pruritus and dyspareunia, white patches, obliteration of the labia minora, and stenosis of the introitus (Figure 2). Histology was conclusive for vulvar LS (Figure 3, a and b). She was successfully treated for 5 months with clobetasol propionate 0.05% ointment. The patient was taking levothyroxine to treat hypothyroidism associated with Hashimoto's thyroiditis and was otherwise healthy. Oral LS is clinically characterized by the appearance of white macules, papules, or plaques mostly appearing on labial mucosa but also on buccal, palate mucosa and on the lower lip (2,3). On the genitals, it typically manifests as atrophic white plaques, which may be accompanied by purpura or fissuring (1). While vulvar LS is often associated with pruritus, dyspareunia, and dysuria, OLS is often asymptomatic, although pain, soreness, pruritus, and tightness when opening the mouth can be present (1,2). Oral manifestations of LS, as well as association of anogenital and oral LS, are rarely reported in the literature (4-6). Tomo et al. searched the Medline database for papers reporting oral LS cases with histological diagnosis confirmation from 1957 to 2016 and found only 34 cases of oral LS with histopathologic confirmation of the diagnosis (4). Kakko et al. reported 39 histologically proven cases of OLS (2). Atilli et al. (5) reviewed the clinical and histologic

features of 72 cases of LS with oral/genital involvement. They reported that LS was diagnosed with exclusive genital lesions in 45, exclusive lip involvement in 20, and orogenital involvement in only 7 cases (5). Some believe that many cases of clinically diagnosed lichen planus may actually be LS and that isolated oral mucosal LS may not be as rare as is generally thought (2). While vulvar LS can occur at any age with increasing incidence with age, the median age of patients with OLS was 34 years and most of the patients were female (1,2,5). Due to the small number of patients in the literature, treatment recommendations for OLS are not available. In case of symptomatic oral lesions, topical or intralesional corticosteroids are considered to be the first-line treatment (2). First-line treatment for anogenital LS is a potent to very potent topical corticosteroid ointment, and second-line therapies include topical calcineurin inhibitors 1% pimecrolimus and 0.1% and 0.03% tacrolimus (1). For treatment-resistant genital LS, oral retinoids, methotrexate, and possibly local steroid injections for single lesions are mainly applicable for women (1). There is limited evidence for systemic treatments for both conditions. If it is not treated, genital LS is associated with a greater degree of scarring and an elevated risk of progression to squamous cell cancer; however, malignant transformation of OLS has not been reported (1-6). Due to the very rare presentation in the oral cavity, it is important to notice these lesions during a dental exam.

Vulvar Diseases, Part I: Approach to the patient.

Mauskar MM, Marathe K, Venkatesan A, Schlosser BJ, Edwards L.

J Am Acad Dermatol. 2019 Nov 8. pii: S0190-9622(19)33012-9. doi: 10.1016/j.jaad.2019.07.115.

<https://www.ncbi.nlm.nih.gov/pubmed/31712174>

Patients with vulvar dermatoses often delay seeking medical treatment due to anxiety and embarrassment. Moreover, women frequently self-treat with various home remedies and see multiple clinicians before presenting to a dermatologist. Despite serving as the primary providers for patients with vulvovaginal symptoms, gynecologists typically receive limited training in the causes and management of these conditions. Dermatologists are experts in the evaluation and management of cutaneous disease and should be the caretakers of all skin, including the genitalia. Vulvar disorders are under-recognized by dermatologists for numerous reasons: inadequate training, lack of comfort with both interview and examination techniques, and unfamiliarity with normal anatomic variations may contribute. Part I of this 2-part series on vulvar dermatoses reviews the fundamentals, approach, and techniques that can be employed to ensure a successful visit for both patient and provider.

Vulvar Diseases Part II: Conditions in adults and children.

Mauskar MM, Marathe K, Venkatesan A, Schlosser BJ, Edwards L.

J Am Acad Dermatol. 2019 Nov 8. pii: S0190-9622(19)33011-7. doi: 10.1016/j.jaad.2019.10.077.

<https://www.ncbi.nlm.nih.gov/pubmed/31712170>

The most problematic vulvovaginal conditions are familiar to dermatologists but may exhibit distinct clinical features or medication management due to the anatomic location. Part 2 of this CME will focus on management pearls for treating vulvar diseases. We highlight key conditions such as lichen sclerosus, erosive lichen planus, and vulvodynia. Additionally, we will review conditions that dermatologists may be less familiar with, such as plasma cell vulvitis, desquamative inflammatory vaginitis, vulvar aphthae, and low estrogen states. Nearly one in six women experience undiagnosed and untreated vulvovaginal discomfort at some point in their lives. Physicians who treat vulvar disorders will improve the quality of life of countless women.

Common and critical inflammatory dermatoses every pathologist should know.

Billings SD.

Mod Pathol. 2019 Nov 1. doi: 10.1038/s41379-019-0400-z.

<https://www.ncbi.nlm.nih.gov/pubmed/31676787>

Inflammatory dermatopathology remains a challenging area for surgical pathologists. Yet every surgical pathologist encounters inflammatory dermatoses as part of routine practice. This review will focus on selected diagnoses that are either commonly encountered in the routine practice of surgical pathology or are critically important. The following entities will be covered: spongiotic dermatoses, lichen simplex chronicus, and early lichen sclerosus in the setting of vulvar biopsies, as well as graft versus host disease, Stevens-Johnson syndrome/toxic epidermal necrolysis, granuloma annulare, pyoderma gangrenosum, and calciphylaxis. Practical points and key histologic features will be emphasized.

Pathophysiology, Clinical Manifestations, and Treatment of Lichen Sclerosus: A Systematic Review.

Fergus KB, Lee AW, Baradaran N, Cohen AJ, Stohr BA, Erickson BA, Mmonu NA, Breyer BN.

Urology. 2019 Oct 9. pii: S0090-4295(19)30870-2. doi: 10.1016/j.urology.2019.09.034.

<https://www.ncbi.nlm.nih.gov/pubmed/31605681>

OBJECTIVE: To elucidate current understanding on the pathophysiological mechanism of genital lichen sclerosus (LS), urologic manifestations, and treatment options. **MATERIALS AND METHODS:** The Medline/PubMed and Embase databases were systematically reviewed for publications pertaining to LS. After applying inclusion and exclusion criteria, references were assessed for relevance to the pathophysiology, presentation, and treatment of LS by title and abstract review by 2 independent reviewers, yielding 186 articles for assessment. **RESULTS:** The contemporary understanding of the epidemiology and histology of LS is reviewed herein. Additionally, we explore in detail the 3 hypotheses regarding the pathophysiological mechanism contributing to disease presentation: infectious etiology, primary immune dysregulation, and the isotraumatopic response. We summarize the available biological evidence supporting each hypothesis. This discussion provides context for understanding LS morbidity and may spur new avenues of research. For the clinician, we review the clinical presentation of disease, including the risk of progression to squamous cell carcinoma. The current medical and surgical treatment options are also detailed. **CONCLUSION:** LS remains a potentially insidious disease which may lead to debilitating urinary and sexual dysfunction. Cross disciplinary research should aim for earlier detection, as well as more effective and durable treatment. The exact cause of LS remains unknown.

Establishment of a novel cancer cell line derived from vulvar carcinoma associated with lichen sclerosus exhibiting a fibroblast-dependent tumorigenic potential.

Dongre H, Rana N, Fromreide S, Rajthala S, Bøe Engelsen I, Paradis J, Gutkind JS, Vintermyr OK, Johannessen AC, Bjørge L, Costea DE.

Exp Cell Res. 2019 Oct 23:111684. doi: 10.1016/j.yexcr.2019.111684.

<https://www.ncbi.nlm.nih.gov/pubmed/31654625>

Vulvar squamous cell carcinoma associated with lichen sclerosus (VLS-VSCC) are rare tumors but with higher recurrence and worse prognosis than other types of VSCC. Lack of experimental models has limited the search for better understanding of the biology and development of treatment modalities. In this study, we isolated and characterized primary cells from VSCC (n = 7) and normal vulvar tissue adjacent to tumor (n = 7). Detailed characterization of the novel spontaneously immortalized cell line,

VCC1 revealed a characteristic epithelial morphology in vitro and a well-differentiated keratinizing SCC histology in vivo, closely resembling the tumor of origin. VCC1 expressed higher levels of epithelial-mesenchymal transition markers and higher clonogenic properties as compared to other established non VLS-VSCC cell lines. In vitro 3D organotypic assays and in vivo xenografts revealed a prominent role of cancer-associated fibroblasts in VCC1 invasion and tumor formation. In conclusion, VCC1 mirrored several major VLS-VSCC features and provided a robust experimental tool for further elucidation of VLS-related oncogenesis and drug testing.

The Vulval Disease Quality of Life Index in women with vulval lichen sclerosus correlates with clinician and symptom scores.

Felmingham C, Chan L, Doyle LW, Veysey E.

Australas J Dermatol. 2019 Nov 14. doi: 10.1111/ajd.13197.

<https://www.ncbi.nlm.nih.gov/pubmed/31729009>

BACKGROUND/OBJECTIVES: The Vulval disease Quality of Life Index (VQLI) is a new tool that assesses the burden of vulval disease on quality of life (QoL). Our objective was to assess the correlation between VQLI score and clinician-rated severity scores, overall patient itch/discomfort, disease duration, sexual activity, and age, in vulval lichen sclerosus (VLS) at a vulval disorders clinic. **METHODS:** A retrospective case note review, including consecutive women with VLS who attended the clinic between April and October 2018. Outcome measures include the VQLI score, clinician-rated severity score, and patient symptom score. **RESULTS:** A total of 109 women with VLS were included. On multivariable analysis, there was evidence of a positive relationship between VQLI scores and the total clinician-rated score (mean increase in VQLI score per unit increase in clinician score 1.34, 95% confidence interval [CI] 0.31, 2.38; $P = 0.01$); the relationship was stronger for the cutaneous component. There was little evidence for relationships of the VQLI with the patient's age, sexual activity or time since onset of symptoms. There was strong evidence for a positive relationship between VQLI score and overall itch/discomfort score (mean increase 2.38, 95% CI 1.88, 2.88; $P < 0.001$). New and follow-up data were obtained on sequential visits for 12 women, among whom the VQLI score dropped a mean -2.75 points between visits (95% CI -6.05, 0.55; $P = 0.094$). **CONCLUSION:** The clinician-rated severity correlates with the impact of VLS on QoL. The VQLI captures information included in a patient itch/discomfort score, which can be easily incorporated into routine assessment.