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Vulvodynia

Innervation Changes Induced by Inflammation in the Murine Vagina.

Sharma H, Ji E, Yap P, Vilimas P, Kyloh M, Spencer NJ, Haberberger RV, Barry CM.
Neuroscience. 2017 Dec 30;372:16-26. doi: 10.1016/j.neuroscience.2017.12.026.
<https://www.ncbi.nlm.nih.gov/pubmed/29294338>

Vulvodynia is a prevalent chronic pain disorder associated with high medical costs and often ineffective treatments. The major pathological feature is proliferation of vaginal nerve fibers. This study aimed to develop a highly reproducible animal model to study neuroproliferation in the vagina and aid the identification of appropriately targeted treatments for conditions such as vulvodynia. Mild chronic inflammation was induced using microinjection of complete Freund's adjuvant in the distal vagina of C57Bl/6 mice. Control mice received saline. Inflammation and innervation density were assessed at 7 and 28 days after a single administration or 14 days following repeated administration of complete Freund's adjuvant or saline. Histochemistry and blinded-analysis of images were used to assess vaginal morphology (H & E) and abundance of macrophages (CD68-labeling), mast cells (toluidine blue staining, mast cell tryptase-immunoreactivity), blood vessels (α SMA-immunoreactivity) and nerve fibers immunoreactive for the pan-neuronal marker PGP9.5. Subpopulations of nerve fibers were identified using immunoreactivity for calcitonin gene-related peptide (CGRP), substance P (SP), vasoactive intestinal peptide (VIP) and neuropeptide Y (NPY). Single administration of complete Freund's adjuvant resulted in vaginal swelling, macrophage infiltration, vascular proliferation and increased abundance of nerve fibers immunoreactive for CGRP, SP, VIP and/or PGP9.5 but not NPY, evident at seven days. Inflammation further increased following repeated administration of complete Freund's adjuvant but nerve fiber proliferation did not. Nerve fiber proliferation continued to be evident at 28 days. The inter-individual differences within each treatment group were small, indicating that this model may be useful to study mechanisms underlying vaginal nerve fiber proliferation associated with inflammation.

Generalized unprovoked vulvodynia; A retrospective study on the efficacy of treatment with amitriptyline, gabapentin or pregabalin.

van Beekhuizen HJ, Oost J, van der Meijden WI.

Eur J Obstet Gynecol Reprod Biol. 2018 Jan;220:118-121. doi: 10.1016/j.ejogrb.2017.10.026. Epub 2017 Oct 31.

<https://www.ncbi.nlm.nih.gov/pubmed/29202395>

OBJECTIVE: To describe patient characteristics of women diagnosed with generalized unprovoked vulvodynia (GUV) and to estimate efficacy and tolerability of treatment. **MATERIAL AND METHODS:** Retrospective observational study in 241 women who presented with GUV at three vulvar disease clinics in Rotterdam, The Netherlands during 1996-2013. Main outcome was efficacy of amitriptyline, gabapentin or pregabalin treatment. **RESULTS:** The median duration of symptoms was 24 months and median age 62 years (range 36-89). Most of the patients reported a burning sensation, often worsened by sitting, urinating or having intercourse. Treatment with either amitriptyline, gabapentin or pregabalin produced long lasting pain relief in 60% and temporary pain relief in 10%, while treatment was not successful in 30% of the patients. Around 30% of the patients had to stop their medication due to side effects. In 44 of the 241 (18%) women signs of vulvar dermatoses were present that could not explain the symptoms. These women experienced the same therapeutic efficacy as those without any visible abnormalities (chi-square goodness of fit $p=0.49$). **CONCLUSIONS:** Amitriptyline, gabapentin and pregabalin produced long lasting pain relief in most of the women with GUV. The 2015 International Society for the Study of Vulvovaginal Disease nomenclature acknowledges the concomitant presence of vulvar dermatoses and vulvodynia. This enables treatment of both conditions simultaneously, a situation that occurs regularly according to our study. We advocate that women with symptoms of GUV, with or without the presence of vulvar dermatoses, receive a therapeutic trial with drugs such as amitriptyline.

The Vulvar Pain Assessment Questionnaire: Factor Structure, Preliminary Norms, Internal Consistency, and Test-Retest Reliability.

Dargie E, Holden RR, Pukall CF.

J Sex Med. 2017 Dec;14(12):1585-1596. doi: 10.1016/j.jsxm.2017.10.072.

<https://www.ncbi.nlm.nih.gov/pubmed/29198513>

BACKGROUND: The Vulvar Pain Assessment Questionnaire (VPAQ) was developed to assist in the assessment and diagnosis of chronic vulvar pain (vulvodynia). **AIM:** To further establish the psychometric properties of the VPAQ by examining factor structure, test-retest reliability, internal consistency, and scale normative data, and to gather feedback from those with vulvar pain about the usefulness and accessibility of the questionnaire. **METHODS:** 182 participants completed a confidential online study and 70 participated again at time 2 (4 weeks later). **OUTCOMES:** Participants were asked to complete the full VPAQ, which assesses pain characteristics, effects on various parts of their lives, coping strategies used, and romantic partner factors. Additional questions captured sociodemographics and feedback about the instrument. **RESULTS:** Exploratory structural equation modeling indicated that the previously established subscales, except the coping scale, had adequate model fit, and all items loaded significantly onto relevant factors. Pearson product moment correlations ($r = 0.57-0.96$) established strong 4-week test-retest reliability for most subscale scores, and Cronbach α indicated overall acceptable to high internal consistency ($\alpha = 0.56-0.95$). Preliminary norms for the scales are supplied. Approximately half the participants reported an increase in their comfort level in discussing a range of topics after completing the VPAQ. Most participants reported that the length, readability, and range of VPAQ questions were "good" or "excellent." **CLINICAL IMPLICATIONS:**

The results of this study provide further justification for using the VPAQ scales in clinical and research settings, preliminary norms for a vulvar pain population, and suggestions for interpretation. **STRENGTHS AND LIMITATIONS:** This study established the psychometric properties of the VPAQ scales using multiple methods at 2 time points and gathered feedback from participants. However, data were collected online so diagnoses could not be confirmed and more than half the initial sample did not complete the survey at time 2. **CONCLUSION:** The results of this study suggest that most VPAQ subscales (except the coping subscale) have moderate to strong psychometric properties and that the VPAQ is user friendly. Dargie E, Holden RR, Pukall CF. The Vulvar Pain Assessment Questionnaire: Factor Structure, Preliminary Norms, Internal Consistency, and Test-Retest Reliability. *J Sex Med* 2017;14:1585-1596.

Daily Anxiety and Depressive Symptoms in Couples Coping with Vulvodynia: Associations with Women's Pain, Women's Sexual Function and Both Partners' Sexual Distress.

Pâquet M, Rosen NO, Steben M, Mayrand MH, Santerre-Baillargeon M, Bergeron S.

J Pain. 2018 Jan 5. pii: S1526-5900(18)30005-1. doi: 10.1016/j.jpain.2017.12.264.

<https://www.ncbi.nlm.nih.gov/pubmed/29309891>

Vulvodynia is a idiopathic vulvovaginal pain condition that interferes with the sexual and mental health of affected couples. Research has underscored that psychological factors, such as anxiety and depression, are associated with its development and maintenance and related sexual impairment. However, the daily role of anxiety and depressive symptoms in the pain and sexuality outcomes of couples coping with vulvodynia is not well understood. Using a dyadic daily experience method, 127 women ($M_{age} = 26.21$, $SD = 6.24$) diagnosed with vulvodynia and their partners ($M_{age} = 27.44$, $SD = 7.29$) reported on anxiety and depressive symptoms, pain, sexual function and sexual distress over a period of eight weeks. Multilevel modeling was used to examine how daily deviations in anxiety and depressive symptoms from a participant's own mean were associated with pain, sexual function and sexual distress. On days of sexual activity, when women reported higher anxiety and depressive symptoms (compared to their average), they reported greater pain and lower sexual function. On days of sexual activity, when women reported higher depressive symptoms, they reported greater levels of sexual distress, and when partners reported higher anxiety and depressive symptoms, both women and partners reported greater levels of sexual distress. Results suggest that daily anxiety and depressive symptoms play a role in women's experience of vulvodynia-related pain, women's sexual function and the couple's sexual distress. Targeting daily anxiety and depressive symptoms could enhance the efficacy of psychological interventions for vulvodynia.

Provoked Vestibulodynia

Toll-Like Receptor Signaling Contributes to Proinflammatory Mediator Production in Localized Provoked Vulvodynia.

Falsetta ML, Foster DC, Woeller CF, Pollock SJ, Bonham AD, Piekna-Przybylska D, Maggirwar SB, Haidaris CG, Phipps RP.

J Low Genit Tract Dis. 2018 Jan;22(1):52-57. doi: 10.1097/LGT.0000000000000364.

<https://www.ncbi.nlm.nih.gov/pubmed/29271858>

OBJECTIVES: Localized provoked vulvodynia (LPV) afflicts approximately 8% of women in the United States and represents a huge financial, physical, and psychological burden. Women with LPV experience intense pain localized to the vulvar vestibule (area immediately surrounding vaginal opening). We have identified mechanisms involved in the development of LPV whereby vulvar fibroblasts respond to proinflammatory stimuli to perpetuate an inflammatory response that causes pain. However, these mechanisms are not fully elucidated. Therefore, we explored the role of toll-like receptors (TLRs), a class of innate immune receptors that rapidly respond to microbial assaults. **MATERIALS AND METHODS:** To determine whether TLRs are expressed by vulvar fibroblasts and whether these contribute to proinflammatory mediator production and pain in LPV, we examined TLR expression and innate immune responses in fibroblasts derived from painful vestibular regions compared with nonpainful external vulvar regions. **RESULTS:** Human vulvar fibroblasts express functional TLRs that trigger production of inflammatory mediators associated with chronic pain. We focused on the TLR-7-imiquimod proinflammatory interaction, because imiquimod, a ligand of TLR-7, may exacerbate pain in women during treatment of human papillomavirus-associated disease. **CONCLUSIONS:** Human vulvar fibroblasts express a broad spectrum of TLRs (a new finding). A significantly higher TLR-mediated proinflammatory response was observed in LPV case vestibular fibroblasts, and with respect to the imiquimod-TLR 7 interaction, development of chronic vestibular pain and inflammation may be a possible sequelae of treatment of vulvar human papillomavirus-associated disease. Suppressing enhanced TLR-associated innate immune responses to a spectrum of pathogen-associated molecular patterns may represent a new/effective therapeutic approach for vulvodynia.

Inflammatory Renin-Angiotensin System Disruption Attenuates Sensory Hyperinnervation and Mechanical Hypersensitivity in a Rat Model of Provoked Vestibulodynia.

Chakrabarty A, Liao Z, Mu Y, Smith PG.

J Pain. 2017 Dec 25. pii: S1526-5900(17)30768-X. doi: 10.1016/j.jpain.2017.10.006.

<https://www.ncbi.nlm.nih.gov/pubmed/29155208>

Vestibulodynia is characterized by perivaginal mechanical hypersensitivity, hyperinnervation, and abundant inflammatory cells expressing renin-angiotensin system proteins. We developed a tractable rat model of vestibulodynia to further assess the contributions of the renin-angiotensin system. Complete Freund's adjuvant injected into the posterior vestibule induced marked vestibular hypersensitivity throughout a 7-day test period. Numbers of axons immunoreactive for PGP9.5, calcitonin gene-related peptide, and GFR α 2 were increased. Numbers of macrophages and T cells were also increased whereas B cells were not. Renin-angiotensin-associated proteins were abundant, with T cells as well as macrophages contributing to increased renin and angiotensinogen. Media conditioned with inflamed vestibular tissue promoted neurite sprouting by rat dorsal root ganglion neurons in vitro, and this was blocked by the angiotensin II receptor type 2 receptor antagonist PD123319 or by an angiotensin II function blocking antibody. Sensory axon sprouting induced by inflamed tissue was dependent on activity of angiotensin-converting enzyme or chymase, but not cathepsin G. Thus, vestibular Complete Freund's adjuvant injection substantially recapitulates changes seen in patients with provoked vestibulodynia, and shows that manipulation of the local inflammatory renin-angiotensin system may be a useful therapeutic strategy. **PERSPECTIVE:** This study provides evidence that inflammation of the rat vestibule induces a phenotype recapitulating behavioral and cytological features of human vestibulodynia. The model confirms a crucial role of the local inflammatory renin-angiotensin system in hypersensitivity and hyperinnervation. Targeting this system holds promise for developing new nonopioid analgesic treatment strategies.

Facilitators and barriers in the diagnostic process of vulvovaginal complaints (vulvodynia) in general practice: a qualitative study.

Leusink P, Teunissen D, Lucassen PL, Laan ET, Lagro-Janssen AL.

Eur J Gen Pract. 2018 Dec;24(1):92-98. doi: 10.1080/13814788.2017.1420774.

<https://www.ncbi.nlm.nih.gov/pubmed/29359605>

BACKGROUND: The gap between the relatively high prevalence of provoked vulvodynia (PVD) in the general population and the low incidence in primary care can partly be explained by physicians' lack of knowledge about the assessment and management of PVD. **OBJECTIVES:** To recognize barriers and facilitators of GPs in the diagnostic process of women presenting with recurrent vulvovaginal complaints. **METHODS:** A qualitative focus group study in 17 Dutch GPs, five men and 12 women. An interview guide, based on the scientific literature and the expertise of the researchers, including a vignette of a patient, was used to direct the discussion between the GPs. The interviews were audiotaped and transcribed verbatim. A systematic text analysis of the transcripts was performed after data saturation was reached. **RESULTS:** Analysis of the interviews generated three major themes: Identifying and discussing sexual complaints, importance of gender in professional experience, and coping with professional uncertainty. Within these themes, the reluctance regarding sexual complaints, male gender, negative emotional responses when faced with professional uncertainty, as well as lack of education were barriers to the diagnostic process and management of PVD. Female gender and understanding that patients can profit from enquiring about sexual health issues were found to be facilitating factors. **CONCLUSIONS:** To improve the care for women with PVD, attitude and skills of GPs regarding taking a sexual history and performing a vulvovaginal examination should be addressed, as well as GPs' coping strategies regarding their professional uncertainty.

Does Self-compassion Benefit Couples Coping with Vulvodynia? Associations with Psychological, Sexual, and Relationship Adjustment.

Santerre-Baillargeon M, O Rosen N, Steben M, Myriam P, Macabena Perez R, Bergeron S.

Clin J Pain. 2017 Dec 21. doi: 10.1097/AJP.0000000000000579.

<https://www.ncbi.nlm.nih.gov/pubmed/29271798>

OBJECTIVES: Vulvodynia, a chronic vulvovaginal pain condition, has deleterious consequences for the psychological, relational, and sexual well-being of affected women and their partners. Protective factors, which can reduce these negative effects, are increasingly studied in the field of chronic pain. One of these, self-compassion, entails qualities such as kindness toward oneself, and has been associated with better adjustment in individuals with chronic pain. Because many women with vulvodynia have a negative image of themselves in the context of sexuality, self-compassion may be especially relevant for this population. This study aimed to investigate self-compassion among couples coping with vulvodynia and its associations with psychological, sexual, and relationship adjustment, as well as pain during sexual intercourse. **METHODS:** Data were gathered from 48 women diagnosed with provoked vestibulodynia—a subtype of vulvodynia—and their partners, using self-report questionnaires pertaining to anxiety, depression, sexual distress, relationship satisfaction and pain intensity during sexual intercourse. **RESULTS:** For both women and their partners, higher levels of self-compassion were associated with their own lower anxiety and depression. When partners reported higher levels of self-compassion, they were more satisfied with their relationship, and both partners and women reported lower sexual distress. No significant association was found for pain during intercourse. **DISCUSSION:** Findings suggest that self-compassion is a promising protective factor in the experience of vulvodynia and associated distress. Interventions aimed at increasing self-compassion

could enhance the efficacy of psychological treatments for these women and their partners. Further studies are needed to better understand the correlates of self-compassion among this population.

Co-morbid Disorders

Vulvar vestibular effects of ospemifene: a pilot study.

Murina F, Di Francesco S, Oneda S.

Gynecol Endocrinol. 2018 Jan 15:1-5. doi: 10.1080/09513590.2018.1427717

<https://www.ncbi.nlm.nih.gov/pubmed/29334798>

The study aimed to assess the effects of ospemifene on vulvar vestibule in postmenopausal women with vulvar pain and dyspareunia. Fifty-five postmenopausal women used oral ospemifene 60 mg/d for 60 d. Symptoms of dryness, burning, and dyspareunia were evaluated on a 10 cm visual analog scale. Visual examination of the vulvar vestibule was also conducted. Patients also underwent current perception threshold (CPT) testing obtained from the vulvar vestibule. Fifty-five patients (94.6%) completed the treatment. Hot flashes were the most frequent adverse effects, but this led to a discontinuation of therapy in three patients (5.4%). After therapy, there was a statistically significant decrease from the baseline in the mean scores for dryness, burning, and dyspareunia and reduction of vestibular trophic score (baseline value of 11.2-4.2 after the therapy, $p \leq 002$) and cotton swab test scores (2.81 compared with 1.25, $p = .001$). There was a difference in CPT values for all nerve fibers and more consistent for C fibers (-38% of sensitivity). These results confirm the efficacy of ospemifene on postmenopausal vestibular symptoms and signs; moreover, the drug was effective in normalizing vestibular innervation sensitivity.

Interpretation of Nondiagnostic Vulvar Biopsies.

Day T, Knight V, Dyall-Smith D, Dennerstein G, Pagano R, Tran H, Tan Y, Yap D, Weigner J, Scurry J

J Low Genit Tract Dis. 2018 Jan;22(1):74-81. doi: 10.1097/LGT.0000000000000366.

<https://www.ncbi.nlm.nih.gov/pubmed/29271860>

OBJECTIVE: The aim of the study was to assess clinical and histopathologic characteristics of symptomatic women who underwent a nondiagnostic biopsy of the inner vulva. **MATERIALS AND METHODS:** Consecutive nondiagnostic biopsies from medial labia minora, posterior fourchette, and vestibule obtained from symptomatic women between 2011 and 2015 were reviewed for this retrospective histopathologic case series. Histopathologic assessment included site, basal layer appearance, lymphocytic infiltrate, and presence of fibrosis or sclerosis. Examination findings, treatment, initial impression, and final clinical diagnosis were recorded. Descriptive statistics were performed; clinical and histopathologic characteristics were compared with Fisher exact test. **RESULTS:** There were 85 cases; mean age was 53 years. Most women presented with painful erythema and underwent biopsy to confirm (30, 35%) or exclude (43, 51%) lichen planus. After clinical follow-up and histopathologic review, most cases had persistent diagnostic discordance. Final clinical diagnoses were available in 70 women: lichen planus in 27 (38%), vulvodynia in 15 (21%), and the other 28 (40%) had LS (8), plasma cell vulvitis (5), psoriasis (4), dermatitis (4), candidosis (3), estrogen deficiency (3), and aphthosis (1). Histopathologic review highlighted the difficulty in distinguishing mucosa-associated lymphoid tissue from an inflammatory infiltrate in 23 (27%) of cases. Compared with other sites, biopsies from the mucocutaneous junction were more likely to be associated with a positive culture for

Candida albicans. **CONCLUSIONS:** Nondiagnostic biopsies from the inner vulva should prompt thoughtful multidisciplinary review, but more research is required to resolve the problem of clinicopathologic discordance through better understanding of vulvar histology and pathophysiology.

Translabial US and Dynamic MR Imaging of the Pelvic Floor: Normal Anatomy and Dysfunction.

Chamié LP, Ribeiro DMFR, Caiado AHM, Warmbrand G, Serafini PC.

Radiographics. 2018 Jan-Feb;38(1):287-308. doi: 10.1148/rg.2018170055.

<https://www.ncbi.nlm.nih.gov/pubmed/29320316>

Pelvic floor dysfunction (PFD) is a common condition that typically affects women older than 50 years and decreases the quality of life. Weakening of support structures can involve all three pelvic compartments and cause a combination of symptoms, including constipation, urinary and fecal incontinence, obstructed defecation, pelvic pain, perineal bulging, and sexual dysfunction. The causes of PFD are complex and multifactorial; however, vaginal delivery is considered a major predisposing factor. Physical examination alone is limited in the evaluation of PFD; it frequently leads to an underestimation of the involved compartments. Imaging has an important role in the clinical evaluation, yielding invaluable information for patient counseling and surgical planning. Three- and four-dimensional translabial ultrasonography (US) is a relatively new imaging modality with high accuracy in the evaluation of PFD such as urinary incontinence, pelvic organ prolapse, and puborectalis avulsion. Evaluation of mesh implants is another important indication for this modality. Dynamic magnetic resonance (MR) imaging of the pelvic floor is a well-established modality for pelvic floor evaluation, with high-resolution images yielding detailed anatomic information and dynamic sequences yielding functional data. Specific protocols and dedicated image interpretation are required with both of these imaging methods. In this article, the authors review the normal anatomy of the female pelvic floor by using a practical approach, discuss the roles of translabial US and MR imaging in the investigation of PFD, describe the most appropriate imaging protocols, and illustrate the most common imaging findings of PFD in the anterior, middle, and posterior compartments of the pelvis. Online supplemental material is available for this article

A Case-Crossover Study of Urologic Chronic Pelvic Pain Syndrome Flare Triggers in the Mapp Research Network.

Sutcliffe S, Jemielita T, Lai HH, Andriole GL, Bradley CS, Clemens JQ, Gallop R, Hooton TM, Kreder KJ, Krieger JN, Kusek JW, Labus J, Lucia MS, Mackey S, Naliboff BD, Robinson NA, Rodriguez LV, Stephens-Shields A, van Bokhoven A, Wolin KY, Yan Y, Yang CC, Landis JR, Colditz GA; MAPP Research Network.

J Urol. 2017 Dec 27. pii: S0022-5347(17)78185-2. doi: 10.1016/j.juro.2017.12.050.

<https://www.ncbi.nlm.nih.gov/pubmed/29288643>

PURPOSE: Although many factors have been proposed to trigger symptom exacerbations ("flares") in patients with interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome, few studies have investigated these factors empirically. Therefore, we embedded a case-crossover study in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain longitudinal study to evaluate a range of patient-reported triggers. **MATERIALS AND METHODS:**

Exposure to proposed triggers (diet, physical activities, sedentary behaviors, stress, sexual activities, infection-like symptoms, and allergies) was assessed by questionnaire a maximum of three times when participants reported flares and at three randomly-selected times. Participants' pre-flare to -non-flare

exposures were compared by conditional logistic regression. **RESULTS:** In our full analytic sample (n=292 participants), only two factors, recent sexual activity (odds ratio (OR)=1.44, 95% confidence interval (CI): 1.06-1.96) and symptoms of a urinary tract infection (OR=3.39, 95% CI: 2.02-5.68), which may overlap with those of flares, were associated with flare onset. In sub-analyses restricted to flares with specific, suspected triggers, additional positive associations were observed for some (certain dietary factors, abdominal muscle exercises, and vaginal infection-like symptoms and fever), but not other (e.g., stress) factors. **CONCLUSIONS:** With the exception of sexual activity, our findings suggest that patient-reported triggers may be either individual/group-specific or may not contribute to flares. These findings suggest caution in following rigid, global flare prevention strategies and support additional research to develop evidence-based strategies.

Vaginal Laxity, Sexual Distress, and Sexual Dysfunction: A Cross-Sectional Study in a Plastic Surgery Practice.

Qureshi AA, Sharma K, Thornton M, Myckatyn TM, Tenenbaum MM.

Aesthet Surg J. 2018 Jan 23. doi: 10.1093/asj/sjx255.

<https://www.ncbi.nlm.nih.gov/pubmed/29370358>

BACKGROUND: Sexual health issues can be characterized by vaginal laxity (VL), sexual distress, and sexual dysfunction. The epidemiology of these issues in plastic surgery patients, and especially breast cancer survivors, remains poorly understood. **OBJECTIVES:** To prospectively assess sexual health issues in a plastic surgery patient population with and without breast cancer. **METHODS:** A prospective cohort study was created in our practice from June to August 2017 with administration of a survey including the vaginal laxity questionnaire (VLQ), female sexual distress scale-revised (FSDS-R), and female sexual function index (FSFI). Multivariate logistic regression identified the controlled effect of patient variables on development of sexual health issues. **RESULTS:** Of 291 patients solicited, 239 completed the survey (37.7% breast cancer survivors vs 62.3% without). Prevalence of VL was nearly 1 in 6 women. Of these, 46.0% met criteria for sexual distress (FSDS-R \geq 11.0) and 64.8% had sexual dysfunction (FSFI \leq 26.5). Breast cancer survivors exhibited significantly greater overall sexual dysfunction (P < 0.001) and greater dysfunction within all FSFI domains of desire, arousal, lubrication, orgasm, satisfaction, and pain (all P < 0.02). On multivariate regression, number of vaginal deliveries predicted development of VL (OR 1.87, P < 0.001), presence of VL predicted sexual distress (OR 3.01, P = 0.007), while history of breast cancer predicted sexual dysfunction (OR 1.87, P < 0.05). **CONCLUSIONS:** Sexual health issues are prevalent amongst plastic surgery patients. Aesthetic practices can improve patients' quality of life by focusing on these areas. Potential therapeutic options to address sexual health issues should consider addressing vaginal laxity.

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

Berghmans B.

Int Urogynecol J. 2018 Jan 9. doi: 10.1007/s00192-017-3536-8.

<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.

History of the Treatment of Female Sexual Dysfunction(s).

Kleinplatz PJ.

Ann Rev Clin Psychol. 2018 Jan 22. doi: 10.1146/annurev-clinpsy-050817-084802.

<https://www.ncbi.nlm.nih.gov/pubmed/29356577>

This article reviews the history of the treatment of women's sexual problems from the Victorian era to the twenty-first century. The contextual nature of determining what constitutes female sexual psychopathology is highlighted. Conceptions of normal sexuality are subject to cultural vagaries, making it difficult to identify female sexual dysfunctions. A survey of the inclusion, removal, and collapsing of women's sexual diagnoses in the Diagnostic and Statistical Manual of Mental Disorders from 1952 to 2013 illuminates the biases in the various editions. Masters and Johnson's models of sexual response and dysfunction paved the way for the diagnosis and treatment of women's sexual dysfunctions. Their sex therapy paradigm is described. Conceptions of and treatments for anorgasmia, arousal difficulties, vaginismus, dyspareunia, and low desire are reviewed. The medicalization of human sexuality and the splintering of sex therapy are discussed, along with current trends and new directions in sexual health care for women. Expected final online publication date for the Annual Review of Clinical Psychology Volume 14 is May 7, 2018. Please see <http://www.annualreviews.org/page/journal/pubdates> for revised estimates.

Pudendal Neuralgia

Dual Site Pudendal Nerve Infiltration: More than Just a Diagnostic Test?

Kastler A, Puget J, Tiberghien F, Pellat JM, Krainik A, Kastler B.

Pain Physician. 2018 Jan;21(1):83-90.

<https://www.ncbi.nlm.nih.gov/pubmed/29357337>

BACKGROUND: Pudendal neuralgia (PN) is a very painful and often disabling condition in which pudendal nerve blocks play an important role in both the diagnosis and management of PN. Some previous reports have advocated the use of pudendal nerve infiltration (PNI) as a diagnostic test

only. **OBJECTIVE:** We aim to assess the outcomes of patients with typical refractory PN who underwent dual site computed tomography (CT)-guided pudendal nerve infiltration. **STUDY DESIGN:** A bicentric, retrospective cohort analysis. **SETTING:** An academic practice. **METHODS:** Between 2002 and 2016, 385 PNIs were performed in 195 patients in the 2 units. Only patients suffering from typical clinical PN were included, and only the first infiltration in each patient was considered for analysis. Therefore, 95 patients who underwent 155 procedures were assessed. Pain was assessed using a visual analog scale (0-10) and self-reported estimated improvement (SRI), expressed as a percentage. Efficacy of the procedure was assessed at 1, 3, and 6 months after procedure follow-up, and clinical success was defined as a 50% decrease of the VAS score. All procedures were performed under CT guidance and on an outpatient basis. Dual site infiltration was performed in each case at both the ischial spine and intra-Alcock's canal sites using a mixture of fast- and slow-acting anesthetic (1 mL lidocaine hydrochloride 1% and 2 mL ropivacaine chlorhydrate) along with a half dose of 1.5 mL of cortivazol (3.75 mg). **RESULTS:** Clinical success at one month post-procedure was present in 63.2% of patients (60/95) with a mean VAS score of 2.07 ($P < 0.05$) and a mean SRI of 71%. At 3 months follow-up, clinical success was still present in 50.5% of patients (48/95) with a mean VAS score of 2.90/10 ($P < 0.05$) and a mean SRI of 62.3%. At 6 months follow-up, the efficacy rate decreased to 25.2% with a mean VAS score of 3.2/10 and SRI of 60%. **LIMITATIONS:** The retrospective aspect of the study is a limitation, as well as the lack of a control group. **CONCLUSION:** Dual site PNI under CT guidance may offer significant mid-term pain relief to a majority of patients suffering from typical refractory PN.

Dermatological Conditions

Gender differences in genital lichen sclerosis.

Virgili A, Borghi A, Cazzaniga S, DI Landro A, Naldi L, Minghetti S, Fierro MT, Verrone A, Caproni M, Micali G, Gaspari V, Papini M, DI Lernia V, Germi L, Girolomoni G, Belloni Fortina A, Cannavò SP, Bilenchi R, Corazza M; GLS Italian Study Group.

G Ital Dermatol Venereol. 2018 Jan 24. doi: 10.23736/S0392-0488.17.05819-9.

<https://www.ncbi.nlm.nih.gov/pubmed/29368855>

BACKGROUND: Studies specifically conducted to assess gender differences in genital lichen sclerosis (GLS) are not available. This multicenter study aimed to identify possible gender-related differences on GLS clinical features, history and course, through collecting data from a large mixed-sex sample of patients. **METHODS:** This was a cross-sectional study on 729 subjects (53.8% females, 46.2% males) affected with GLS, consecutively observed within a network of 15 Italian dermatology units. The following information was specifically collected: clinical features and severity of symptoms related to GLS, extragenital involvement, previous therapies, diagnostic suspicion at referral, type of referring physicians, development of genital squamous-cell carcinoma (SCC). **RESULTS:** Females complained of symptoms more frequent and severe than men; pallor and scarring-sclerosis-atrophy were the most frequent features without gender differences; itching-related signs were more frequent in females than in males as well as extragenital involvement; prior to receiving a definitive diagnosis, females received treatment more frequently than males; 40% of patients were referred with a misdiagnosis; the highest rate of correct suspected diagnosis at referral came from dermatologists than from other physicians; duration of the disease was found to predispose to SCC development. **CONCLUSIONS:** Our findings highlighted several gender differences on clinical presentation and symptom profile of GLS. In spite of some characteristic features, misdiagnosis at referrals was frequent.

Dyspareunia in vulvar lichen sclerosus: an overview of a distressing symptom.

Corazza M, Virgili A, Minghetti S, Borghi A.

G Ital Dermatol Venereol. 2017 Dec 15. doi: 10.23736/S0392-0488.17.05849-7.

<https://www.ncbi.nlm.nih.gov/pubmed/29249126>

BACKGROUND: Dyspareunia is a symptom of vulvar lichen sclerosus (VLS). This study specifically addressed prevalence and severity of dyspareunia in patients affected with VLS as well as the factors that can influence its occurrence. Changes in the severity of dyspareunia with treatment were also explored. **METHODS:** In this retrospective, cohort study we included VLS patients who had undergone any topical treatment for 12 weeks, between January 2011 and March 2016, at our Vulva Unit; demographics, history and clinical features recorded at baseline and at treatment completion were elaborated. **RESULTS:** 177 patients were included; among the 90 patients who reported having sexual activity 56.7% complained of dyspareunia; the frequency and severity of dyspareunia was higher among the patients who had not previously been treated with topical corticosteroids than among those who had undergone previous treatments; the patients complaining of dyspareunia reported significantly higher scores for itching and burning compared with those who did not have painful intercourses; after the treatment, 52.5%, 78.4% and 64.3% of the patients reported an improvement $\geq 75\%$ compared with baseline in dyspareunia, itching and burning scores, respectively.

CONCLUSIONS: Dyspareunia occurred in more than half VLS patients. The patients who complained of dyspareunia had a more severe overall symptom profile than those who did not report having painful intercourses. The objective severity of VLS did not seem to significantly affect dyspareunia occurrence and severity. Dyspareunia was found to be the symptom most resistant to treatment, however early treatment can be expected to reduce its occurrence and severity.

Development of the Adult Vulvar Lichen Sclerosus Severity Scale-A Delphi Consensus Exercise for Item Generation.

Sheinis M, Selk A.

J Low Genit Tract Dis. 2018 Jan;22(1):66-73. doi: 10.1097/LGT.0000000000000361.

<https://www.ncbi.nlm.nih.gov/pubmed/29095746>

OBJECTIVE: To generate a list of items through international expert consensus consisting of both symptoms and clinical signs for inclusion in an adult vulvar lichen sclerosus severity scale. **METHODS:** This study was carried out as a three-stage Delphi consensus exercise. After an extensive literature review, any items used to determine disease severity in previous clinical trials were compiled into a survey. The Delphi participants were recruited from the International Society for the Study of Vulvovaginal Disease most of whom were gynecologists and in practice for more than 20 years. Participants were asked to rate the importance of these items. Consensus was defined as 75% agreeing that an item was very important or essential toward determining disease severity. Participants were also asked to indicate preferred method of measurement for these items. **RESULTS:** Of approximately 400 members of the International Society for the Study of Vulvovaginal Disease, 66 participated in the study. Of the 14 symptoms presented, 7 reached consensus for inclusion. Of the 23 signs presented, 11 reached consensus for inclusion and 1 reached consensus for exclusion. Of the six architectural changes presented, all six reached consensus for inclusion. No consensus was reached regarding method of measurement for any of the symptoms and signs that reached consensus for inclusion. **CONCLUSION:** International consensus was reached for a variety of items for use in an adult vulvar lichen sclerosus severity scale that will be further developed and tested. Ideally, this scale will be used in clinical practice and in research to allow for high-quality trials.

Photodynamic Therapy for Vulvar Lichen Sclerosus-A Systematic Review.

Prodromidou A, Chatziioannou E, Daskalakis G, Stergios K, Pergialiotis V.

J Low Genit Tract Dis. 2018 Jan;22(1):58-65. doi: 10.1097/LGT.0000000000000362.

<https://www.ncbi.nlm.nih.gov/pubmed/29271859>

OBJECTIVE: Lichen sclerosus (LS) is a disease affecting mostly genital and perianal areas. Photodynamic therapy (PDT) has gained interest during the past years. The present study accumulates current evidence on the efficacy of PDT in the management of vulvar LS. **METHODS:** We used Medline (1966-2017), Scopus (2004-2017), ClinicalTrials.gov (2008-2017) and Cochrane Central Register of Controlled Trials CENTRAL (1999-2017) databases in our primary search along with the reference lists of electronically retrieved full-text papers. **RESULTS:** Eleven studies were finally included in our systematic review, which recruited 337 women. The existing evidence supports that PDT results in significant relief of symptoms related to LS, hence remains confusing in evaluating the progress in the clinical appearance of the lesion. No major adverse effects were reported during therapy and during the posttreatment period. Pathologic findings seem to be conflicting, as current data do not unanimously support a beneficial histological effect. **CONCLUSIONS:** According to the findings of our study, PDT seems to be promising in the treatment of patients with vulvar LS. Nonetheless, current knowledge is extremely limited, and further observational studies with large patient series are needed in the field to elucidate the efficacy of PDT.

Cancer risk of Lichen planus: A cohort study of 13,100 women in Finland.

Halonen P, Jakobsson M, Heikinheimo O, Riska A, Gissler M, Pukkala E.

Int J Cancer. 2018 Jan 1;142(1):18-22. doi: 10.1002/ijc.31025. Epub 2017 Sep 8.

<https://www.ncbi.nlm.nih.gov/pubmed/28857160>

The association between Lichen planus (LP) and cancer has been under debate for decades. We studied the connection via population-based Finnish register data. All women with the diagnosis of LP (n = 13,100) were identified from the Finnish Hospital Discharge Registry from 1969-2012. These patients were linked with subsequent cancer diagnoses from the Finnish Cancer Registry until 2014. Standardized incidence ratios (SIRs) were counted for different cancers by dividing the observed numbers of cancers by expected numbers, which were based on national cancer incidence rates. In total, 1,520 women with LP were diagnosed with cancer (SIR 1.15, 95% confidence interval [CI] 1.09-1.20). LP was associated with an increased risk of cancer of lip (SIR 5.17, 95% CI 3.06-8.16), cancer of tongue (SIR 12.4, 95% CI 9.45-16.0), cancer of oral cavity (SIR 7.97, 95% CI 6.79-9.24), cancer of esophagus (SIR 1.95, 95% CI 1.17-3.04), cancer of larynx (SIR of 3.47, 95% CI 1.13-8.10) and cancer of vulva (SIR 1.99, 95% CI 1.18-3.13). The risk of cancer was not increased in other locations where LP manifests (pharynx and skin). Patients with diagnosed LP have an increased risk of developing cancer of lip, tongue, oral cavity, esophagus, larynx and vulva. These data are important when considering treatment and follow-up of patients with LP diagnosis.

MiR-155-5p promotes fibroblast cell proliferation and inhibits FOXO signaling pathway in vulvar lichen sclerosis by targeting FOXO3 and CDKN1B.

Ren L, Zhao Y, Huo X, Wu X.

Gene. 2018 Jan 12. pii: S0378-1119(18)30056-8. doi: 10.1016/j.gene.2018.01.049.

<https://www.ncbi.nlm.nih.gov/pubmed/29339071>

Vulvar lichen sclerosis (VLS) is a chronic inflammatory skin disorder. Evidence is accumulating that microRNAs (miRNAs) exert crucial roles in initiation and development of a wide range of human diseases. MiR-155-5p has been frequently reported to be implicated in the tumorigenesis and progression of multiple types of cancers, however, its biological role in VLS remains unclear. This study aimed to explore the role of miR-155-5p in VLS and clarify the potential molecular mechanisms involved. In the present study, miR-155-5p was observed to be significantly upregulated in VLS tissues. Functional studies showed that miR-155-5p facilitated cell proliferation, accelerated cell cycle progression and inhibited forkhead box O (FOXO) signaling pathway in fibroblast cells. Mechanical studies demonstrated that miR-155-5p exerted its promoting effects on fibroblast cell proliferation via targeting both forkhead box O3 (FOXO3) and cyclin-dependent kinase inhibitor 1B (CDKN1B). Besides, Pearson's correlation analysis revealed that miR-155-5p expression was negatively correlated with the mRNA expression of FOXO3 and CDKN1B in VLS tissues. Taken together, our results indicate that miR-155-5p promotes fibroblast cell proliferation and inhibits FOXO signaling pathway by negative modulation of both FOXO3 and CDKN1B in VLS, and that miR-155-5p may be used to be a potential therapeutic target for VLS.

[Lichen sclerosis : Symptoms, diagnosis, therapeutic procedures].

[Article in German]

Kirtschig G.

Hautarzt. 2018 Jan 16. doi: 10.1007/s00105-017-4121-2.

<https://www.ncbi.nlm.nih.gov/pubmed/29340709>

Lichen sclerosis is a chronic, inflammatory dermatosis that usually affects the anogenital area. Early diagnosis and subsequent long-term anti-inflammatory treatment may reduce symptoms and signs and the risk of a mutilating course and the development of carcinomas.

Diagnosis and Treatment of Vulvar Dermatoses.

Stockdale CK, Boardman L.

Obstet Gynecol. 2018 Feb;131(2):371-386. doi: 10.1097/AOG.0000000000002460.

<https://www.ncbi.nlm.nih.gov/pubmed/29324620>

Vulvar symptoms of pain, dyspareunia, and pruritus are common and may significantly affect a woman's sense of well-being and sexual function. Despite this, vulvar symptoms are often underreported by women. When identified, however, vulvovaginal symptoms should be addressed by health care providers to optimize care. The evaluation of patients with vulvovaginal complaints begins with a thorough history and physical examination. Biopsy is indicated when concern exists for malignancy or the diagnosis is uncertain. Treatment, if possible, should be evidence-based, although for many vulvar disorders including vulvardermatoses, treatment is based on limited evidence and anecdotal experience. Although many vulvar dermatoses represent chronic conditions and thus cannot be simply cured, control is possible for the majority of women. Patient education regarding vulvar hygiene and skin care is the foundation for optimal management of inflammatory vulvar dermatoses. These conditions may be triggered or worsened by aggressive hygiene. Additionally, patients should be counseled regarding the need for individually tailored long-term maintenance to achieve optimal outcomes.

Vitiligoid variant of lichen sclerosus in young girls with darker skin types.

Dennin MH, Stein SL, Rosenblatt AE.

Pediatr Dermatol. 2018 Jan 4. doi: 10.1111/pde.13399.

<https://www.ncbi.nlm.nih.gov/pubmed/29314207>

BACKGROUND/OBJECTIVES: Vitiligo and lichen sclerosus are autoimmune disorders characterized by white discoloration, and both frequently affect the anogenital region. Vitiligoid lichen sclerosus refers to a superficial variant of lichen sclerosus in which the lesion appears clinically to be vitiligo based on the predominant presentation of depigmentation and minimal inflammation and sclerosis but histologically is consistent with lichen sclerosus. A limited number of reports have described vitiligoid lichen sclerosus, and from these reports, it appears to primarily affect darker-skinned people.

METHODS: We retrospectively reviewed the records of 7 girls with darker skin types seen in our pediatric dermatology clinic who presented with a clinical overlap of vitiligo and lichen sclerosus. All had primarily well-demarcated, depigmented patches characteristic of vitiligo, but the lesions were symptomatic (pruritus, pain, bleeding, constipation), a presentation more consistent with lichen sclerosus. **RESULTS:** The girls were all treated with high-potency topical steroids, calcineurin inhibitors, or both. The associated symptoms improved or resolved, but most had minimal improvement of the depigmentation. **CONCLUSIONS:** The girls presented in this series appear to have had vitiligoid lichen sclerosus, given the clinical overlap of lichen sclerosus and vitiligo affecting the anogenital region, particularly given that they did not have depigmented patches elsewhere on their body. Previous cases of vitiligoid lichen sclerosus have been reported in darker skin types, and our findings support this possible predisposition. It is important for clinicians to assess patients presenting with genital depigmentation for overlapping features of vitiligo and lichen sclerosus and determine appropriate management.

5-Aminolevulinic acid photodynamic therapy in refractory vulvarlichen sclerosus et atrophicus: series of ten cases.

Lan T, Zou Y, Hamblin MR, Yin R.

Photodiagnosis Photodyn Ther. 2017 Dec 16. pii: S1572-1000(17)30529-X. doi:

10.1016/j.pdpdt.2017.12.003.

<https://www.ncbi.nlm.nih.gov/pubmed/29258952>

BACKGROUND: Vulvar lichen sclerosus et atrophicus (VLSA) is a chronic inflammatory skin disease of unknown etiology that mainly affects postmenopausal and perimenopausal women. The primary clinical symptoms of VLSA are itching, burning pain, and dyspareunia that can result in decreased quality of life. Existing therapies including topical corticosteroid ointment, topical calcineurin inhibitors, estrogens, are not very effective for treatment of VLSA. **OBJECTIVE:** To evaluate the effectiveness and safety of 5-aminolevulinic acid mediated photodynamic therapy (ALA-PDT) in the treatment of VLSA.

MATERIALS AND METHODS: Ten patients with VLSA who had failed conventional treatment received ALA-PDT. 10% 5-ALA in an oil-in-water emulsion was applied to the lesions and occluded with plastic film for 3 h, when the lesions were irradiated with 100 mW/cm², 635 ± 15 nm red light for 20 minutes. Treatments were repeated three times at 2-week intervals. Objective and subjective symptoms and signs of the vulvar lesions based on horizontal visual analogue scales were recorded at each treatment and 1, 3, and 6 months after the last session. The quality of life was assessed using dermatology life quality index (DLQI) questionnaire. **RESULTS:** All patients completed three ALA-PDT treatments and the follow-up visits. Clinical symptoms of itching disappeared completely in nine patients, one patient had

itching decreased from severe to mild. All subjects showed objective improvement in lesions. The DLQI of all cases improved after treatment. The main side-effects of ALA-PDT were pain, erythema, and swelling. Side-effects were transient and tolerable. All patients reported being "satisfied" or "very satisfied" with their outcomes. **CONCLUSIONS:** ALA-PDT is an effective and safe approach for the treatment of VLSA.