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Feature Article

Vulvodynia-An Evidence-Based Literature Review and Proposed Treatment Algorithm.

De Andres J, Sanchis-Lopez N, Asensio-Samper JM, Fabregat-Cid G, Villanueva-Perez VL, Monsalve Dolz V, Minguez A.

Pain Pract. 2015 Jan 12. doi: 10.1111/papr.12274.

http://www.ncbi.nlm.nih.gov/pubmed/25581081

OBJECTIVE: We searched the medical literature from the last 15 years (1998 to 2013) relating to the etiology, diagnosis, and treatment of vulvodynia. The evidence was reviewed supporting the therapeutic proposals currently in use and propose the incorporation of novel, minimally invasive, interventional therapies, within the context of a multidisciplinary approach. **METHODS:** This was a systematic review of all relevant studies with no language restrictions. Studies were identified through Medline/PubMed (1998 to March 2013), the Cochrane Library (2001 to 2013), and conference records and book chapters. The keywords used included "chronic pelvic pain," "vulvodynia," "vestibulodynia," and search terms "etiology," "diagnosis," and "treatment" were added. The levels of evidence were assessed using grading system for "Therapy/Prevention/Etiology/Harm" developed by the Centre for Evidence-Based Medicine (CEBM). The grading system assists in clinical decision-making, and we decided to use "The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)." **RESULTS:** A total of 391 papers were assessed. Of these, 215 were analyzed and 175 were excluded, as they pertained to areas not directly related to the disease under review. **CONCLUSION:** The optimal therapy for vulvar pain syndrome remains elusive, with low percentages of therapeutic success, using either local or systemic pharmacological approaches. Surgery involving invasive and often irreversible therapeutic procedures has resulted in success for certain subtypes of vulvodynia. We present a multidisciplinary approach whereby pain treatment units may provide an intermediate level of care between standard medical and surgical treatments.

Vulvodynia/Vulvovaginal Pain

Pelvic floor muscle function in women with provoked vestibulodynia and asymptomatic controls.
Næss I, Bø K.
Int Urogynecol J. 2015 Mar 4.
http://www.ncbi.nlm.nih.gov/pubmed/25735988

INTRODUCTION AND HYPOTHESIS: The purpose of the present study was to assess vaginal resting pressure (VRP), pelvic floor muscle (PFM) strength and endurance, and surface EMG activity in women with and without provoked vestibulodynia (PVD). **METHODS:** This was an assessor-masked comparison study including 70 women. Exclusion criteria were any previous pregnancy and presence of candida. Sensitivity of the vulvar vestibule was rated at three sites with Q-tip pressure measurement and a numerical rating scale for pain. VRP and PFM strength and endurance were measured with a high precision pressure transducer connected to a vaginal balloon. Pelvic floor muscle activity was measured with surface EMG. The independent samples t test was used to analyze differences between groups. The p value was set to <0.05 RESULTS: The mean age of the participants was 24.3 years (SD 4.7) and mean body mass index (BMI) was 22.0 kg/m^2 (SD 2.6). Q-tip pressure measurement was significantly lower and pain more severe in the PVD group at all sites of the vulvar vestibule. The PVD group had significantly higher VRP: 20.6 cmH_2O (SD 7.1) versus controls: 17.3 cmH_2O (SD 4.4), p = 0.02. The PVD group had significantly lower muscle activity during a 10-s holding period; PVD: 465.2 µV (SD 218.4), controls: 591.1 µV (SD 277.7), p = 0.04. **CONCLUSION:** Young, nulliparous women with PVD had significantly higher VRP, but this finding was not confirmed by vaginal surface EMG.

Transcutaneous electrical nerve stimulation as an additional treatment for women suffering from therapy-resistant provoked vestibulodynia: a feasibility study.
Vallinga MS, Spoelstra SK, Hemel IL, van de Wiel HB, Weijmar Schultz WC.
J Sex Med. 2015 Jan;12(1):228-37. doi: 10.1111/jsm.12740. Epub 2014 Nov 12.
http://www.ncbi.nlm.nih.gov/pubmed/25388372

INTRODUCTION: The current approach to women with provoked vestibulodynia (PVD) comprises a multidimensional, multidisciplinary therapeutic protocol. As PVD is considered to be a chronic pain disorder, transcutaneous electrical nerve stimulation (TENS) can be used as an additional therapy for women with otherwise therapy-resistant PVD. **AIMS:** The aims of this study were to evaluate whether TENS has a beneficial effect on vulvar pain, sexual functioning, and sexually-related personal distress in women with therapy-resistant PVD and to assess the effect of TENS on the need for vestibulectomy. **METHODS:** A longitudinal prospective follow-up study was performed on women with therapy-resistant PVD who received additional domiciliary TENS. Self-report questionnaires and visual analog scales (VASs) were completed at baseline (T1), post-TENS (T2), and follow-up (T3). **MAIN OUTCOME MEASURES:** Vulvar pain, sexual functioning, and sexually-related personal distress were the main outcome measures. **RESULTS:** Thirty-nine women with therapy-resistant PVD were included. Mean age was 27 ± 5.6 years (range: 19 to 41); mean duration between TENS and T3 follow-up was 10.1 ± 10.7 months (range: 2 to 32). Vulvar pain VAS scores directly post-TENS (median 3.4) and at follow-up (median 3.2) were significantly (P < 0.01) lower than at baseline (median 8.0). Post-TENS, sexual functioning scores on the Female Sexual Functioning Index questionnaire had improved significantly (P = 0.2); these scores remained stable at follow-up. Sexually-related personal distress scores had improved significantly post-TENS (P = 0.01). Only 4% of the women who received TENS needed to undergo vestibulectomy vs. 23%

in our previous patient population. **CONCLUSION:** The addition of self-administered TENS to multidimensional treatment significantly reduced the level of vulvar pain and the need for vestibulectomy. The long-term effect was stable. These results not only support our hypothesis that TENS constitutes a feasible and beneficial addition to multidimensional treatment for therapy-resistant PVD, but also the notion that PVD can be considered as a chronic pain syndrome.

Decreased concentration of protease inhibitors: possible contributors to allodynia and hyperalgesia in women with vestibulodynia.

Jayaram A, Esbrand F, Dulaveris G, Orfanelli T, Sobel R, Ledger WJ, Witkin SS.

Am J Obstet Gynecol. 2015 Feb;212(2):184.e1-4. doi: 10.1016/j.ajog.2014.07.029. Epub 2014 Jul 25.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Am+J+Obstet+Gynecol+2015%3B212%3A184.e1-4

OBJECTIVE: Women with vestibulodynia exhibit increased pain sensitivity to contact with the vaginal vestibule as well as with vaginal penetration. The mechanism(s) responsible for this effect remains incompletely defined. Based on reports of a possible role for proteases in induction of pain, we compared levels of proteases and protease inhibitors in vaginal secretions from women with vestibulodynia and controls. **STUDY DESIGN:** Vaginal secretions from 76 women with vestibulodynia and from 41 control women were assayed by an enzyme-linked immunosorbent assay for the protease inhibitors, secretory leukocyte protease inhibitor (SLPI) and human epididymis protein-4 (HE-4), and the proteases, kallikrein-5 and cathepsins B and S. Concentrations between subjects and controls were compared and levels related to clinical and demographic variables. **RESULTS:** Concentrations of HE-4 and SLPI were markedly reduced in vaginal samples from women with vestibulodynia compared with controls ($P \leq .006$). All other compounds were similar in both groups. HE-4 ($P = .0195$) and SLPI ($P = .0033$) were lower in women with secondary, but not primary, vestibulodynia than in controls. Subjects who had constant vulvar pain had lower levels of HE-4 and SLPI than did healthy control women ($P \leq .006$) or women who experienced vulvar pain only during sexual intercourse ($P \leq .0191$). There were no associations between HE-4 or SLPI levels and event associated with symptom onset, duration of symptoms, age, number of lifetime sexual partners, or age at sex initiation. **CONCLUSION:** Insufficient vaginal protease inhibitor production may contribute to increased pain sensitivity in an undefined subset of women with secondary vestibulodynia who experience constant vulvar pain.

Concurrent deep-superficial dyspareunia: prevalence, associations, and outcomes in a multidisciplinary vulvodynia program.

Yong PJ, Sadownik L, Brotto LA.

J Sex Med. 2015 Jan;12(1):219-27. doi: 10.1111/jsm.12729. Epub 2014 Oct 27.

http://www.ncbi.nlm.nih.gov/pubmed/25345552

INTRODUCTION: Little is known about women with concurrent diagnoses of deep dyspareunia and superficial dyspareunia. **AIM:** The aim of this study was to determine the prevalence, associations, and outcome of women with concurrent deep-superficial dyspareunia. **METHODS:** This is a prospective study of a multidisciplinary vulvodynia program ($n = 150$; mean age 28.7 ± 6.4 years). Women with superficial dyspareunia due to provoked vestibulodynia were divided into two groups: those also having deep dyspareunia (i.e., concurrent deep-superficial dyspareunia) and those with only superficial dyspareunia due to provoked vestibulodynia. Demographics, dyspareunia-related factors, other pain conditions, and psychological variables at pretreatment were tested for an association with concurrent deep-superficial dyspareunia. Outcome in both groups was assessed to 6 months posttreatment. **MAIN**

OUTCOME MEASURES: Level of dyspareunia pain (0-10) and Female Sexual Distress Scale were the main outcome measures. **RESULTS:** The prevalence of concurrent deep-superficial dyspareunia was 44% (66/150) among women with superficial dyspareunia due to provoked vestibulodynia. At pretreatment, on multiple logistic regression, concurrent deep-superficial dyspareunia was independently associated with a higher level of dyspareunia pain (odds ratio [OR] = 1.19 [1.01-1.39], P = 0.030), diagnosis of endometriosis (OR = 4.30 [1.16-15.90], P = 0.022), history of bladder problems (OR = 3.84 [1.37-10.76], P = 0.008), and more depression symptoms (OR = 1.07 [1.02-1.12], P = 0.007), with no difference in the Female Sexual Distress Scale. At 6 months posttreatment, women with concurrent deep-superficial dyspareunia improved in the level of dyspareunia pain and in the Female Sexual Distress Scale to the same degree as women with only superficial dyspareunia due to provoked vestibulodynia. **CONCLUSIONS:** Concurrent deep-superficial dyspareunia is reported by almost half of women in a multidisciplinary vulvodynia program. In women with provoked vestibulodynia, concurrent deep-superficial dyspareunia may be related to endometriosis or interstitial cystitis, and is associated with depression and more severe dyspareunia symptoms. Standardized multidisciplinary care is effective for women with concurrent dyspareunia.

Identification of novel mechanisms involved in generating localized vulvodynia pain.
Falsetta ML, Foster DC, Woeller CF, Pollock SJ, Bonham AD, Haidaris CG, Stodgell CJ, Phipps RP.
Am J Obstet Gynecol. 2015 Feb 12.
http://www.ncbi.nlm.nih.gov/pubmed/25683963

OBJECTIVE: Our goal was to gain a better understanding of the inflammatory pathways affected during localized vulvodynia, a poorly understood, common, and debilitating condition characterized by chronic pain of the vulvar vestibule. **METHODS:** In a control matched study, primary human fibroblast strains were generated from biopsies collected from localized provoked vulvodynia (LPV) cases and age and race-matched controls. We then examined intracellular mechanisms by which these fibroblasts recognize pathogenic Candida albicans; >70% of vulvodynia patients report the occurrence of prior chronic Candida infections, which is accompanied by localized inflammation and elevated production of pro-inflammatory/pain-associated interleukin 6 (IL-6) and prostaglandin E2 (PGE_2). We focused on examining the signaling pathways involved in recognition of yeast components that are present and abundant during chronic infection. **RESULTS:** Dectin-1, a surface receptor that binds C. albicans cell wall glucan, was significantly elevated in vestibular versus external vulvar cells (from areas without pain) in both cases and controls, while its abundance was highest in LPV cases. Blocking Dectin-1 signaling significantly reduced pain-associated IL-6 and PGE_2 production during the response to C. albicans. Furthermore, LPV patient vestibular cells produced inflammatory mediators in response to low numbers of C. albicans cells, while external vulvar fibroblasts were nonresponsive. Inhibition of NFκB (pro-inflammatory transcription factor) nearly abrogated IL-6 and PGE_2 production induced by C. albicans, in keeping with observations that Dectin-1 signals through the NFκB pathway. **CONCLUSION:** These findings implicate that a fibroblast-mediated pro-inflammatory response to C. albicans contributes to the induction of pain in LPV cases. Targeting this response may be an ideal strategy for the development of new vulvodynia therapies.

Genetic differences may reflect differences in susceptibility to vulvodynia in general or in spontaneous remission propensity: a response.
Goldstein AT, Kim N, Burrows LJ, Goldstein I.
J Sex Med. 2015 Feb;12(2):578-9. doi: 10.1111/jsm.12822.
http://www.ncbi.nlm.nih.gov/pubmed/25627974

No abstract available.

Impact of a multidisciplinary vulvodynia program on sexual functioning and dyspareunia.
Brotto LA, Yong P, Smith KB, Sadownik LA.
J Sex Med. 2015 Jan;12(1):238-47. doi: 10.1111/jsm.12718. Epub 2014 Oct 30
http://www.ncbi.nlm.nih.gov/pubmed/25354520

INTRODUCTION: For many years, multidisciplinary approaches, which integrate psychological, physical, and medical treatments, have been shown to be effective for the treatment of chronic pain. To date, there has been anecdotal support, but little empirical data, to justify the application of this multidisciplinary approach toward the treatment of chronic sexual pain secondary to provoked vestibulodynia (PVD). **AIM:** This study aimed to evaluate a 10-week hospital-based treatment (multidisciplinary vulvodynia program [MVP]) integrating psychological skills training, pelvic floor physiotherapy, and medical management on the primary outcomes of dyspareunia and sexual functioning, including distress. **METHOD:** A total of 132 women with a diagnosis of PVD provided baseline data and agreed to participate in the MVP. Of this group, n = 116 (mean age 28.4 years, standard deviation 7.1) provided complete data at the post-MVP assessment, and 84 women had complete data through to the 3- to 4-month follow-up period. **RESULTS:** There were high levels of avoidance of intimacy (38.1%) and activities that elicited sexual arousal (40.7%), with many women (50.4%) choosing to focus on their partner's sexual arousal and satisfaction at baseline. With treatment, over half the sample (53.8%) reported significant improvements in dyspareunia. Following the MVP, there were strong significant effects for the reduction in dyspareunia ($P = 0.001$) and sex-related distress ($P < 0.001$), and improvements in sexual arousal ($P < 0.001$) and overall sexual functioning ($P = 0.001$). More modest but still statistically significant were improvements in sexual desire, lubrication, orgasmic function, and sexual satisfaction. All improvements were retained at 2- to 3-month follow-up. **CONCLUSION:** This study provides strong support for the efficacy of a multidisciplinary approach (psychological, pelvic floor physiotherapy, and medical management) for improving dyspareunia and all domains of sexual functioning among women with PVD. The study also highlights the benefits of incorporating sexual health education into general pain management strategies for this population.

A comparison of cognitive-behavioral couple therapy and lidocaine in the treatment of provoked vestibulodynia: study protocol for a randomized clinical trial.
Corsini-Munt S, Bergeron S, Rosen NO, Steben M, Mayrand MH, Delisle I, McDuff P, Aerts L, Santerre-Baillargeon M.
Trials. 2014 Dec 23;15:506. doi: 10.1186/1745-6215-15-506.
http://www.ncbi.nlm.nih.gov/pubmed/25540035

BACKGROUND: Provoked vestibulodynia (PVD), a frequent form of chronic genital pain, is associated with decreased sexual function for afflicted women, as well as impoverished sexual satisfaction for women and their partners. Pain and sexuality outcomes for couples with PVD are influenced by

interpersonal factors, such as pain catastrophizing, partner responses to pain, ambivalence over emotional expression, attachment style and perceived relationship and sexual intimacy. Despite recommendations in the literature to include the partner in cognitive-behavioral therapy targeted at improving pain and sexuality outcomes, no randomized clinical trial has tested the efficacy of this type of intervention and compared it to a first-line medical intervention. **METHODS:** This bi-center, randomized clinical trial is designed to examine the efficacy of cognitive-behavioral couple therapy compared to topical lidocaine. It is conducted across two Canadian university-hospital centers. Eligible women diagnosed with PVD and their partners are randomized to one of the two interventions. Evaluations are conducted using structured interviews and validated self-report measures at three time points: Pre-treatment (T1: prior to randomization), post-treatment (T2), and 6-month follow-up (T3). The primary outcome is the change in reported pain during intercourse between T1 and T2. Secondary outcomes focus on whether there are significant differences between the two treatments at T2 and T3 on (a) the multidimensional aspects of women's pain and (b) women and partners' sexuality (sexual function and satisfaction), psychological adjustment (anxiety, depression, catastrophizing, self-efficacy, and quality of life), relationship factors (partner responses and dyadic adjustment) and self-reported improvement and treatment satisfaction. In order to detect an effect size as small as 0.32 for secondary outcomes, a sample of 170 couples is being recruited (27% dropout expected). A clinically significant decrease in pain is defined as a 30% reduction. **DISCUSSION:** The randomized clinical trial design is the most appropriate to examine the efficacy of cognitive-behavioral couple therapy, a recently developed and pilot-tested psychosocial intervention for couples coping with PVD, in comparison to a frequent first-line treatment option, topical lidocaine. Findings from this study will provide important information about empirically supported treatment options for PVD, and inform future treatment development and research for this patient population.

The future of research in female pelvic medicine.
Chao J, Chai TC.
Curr Urol Rep. 2015 Feb;16(2):474. doi: 10.1007/s11934-014-0474-6.
http://www.ncbi.nlm.nih.gov/pubmed/25604652

Female pelvic medicine and reconstructive surgery (FPMRS) was recently recognized as a subspecialty by the American Board of Medical Specialties (ABMS). FPMRS treats female pelvic disorders (FPD) including pelvic organ prolapse (POP), urinary incontinence (UI), fecal incontinence (FI), lower urinary tract symptoms (LUTS), lower urinary tract infections (UTI), pelvic pain, and female sexual dysfunction (FSD). These conditions affect large numbers of individuals, resulting in significant patient, societal, medical, and financial burdens. Given that treatments utilize both medical and surgical approaches, areas of research in FPD necessarily cover a gamut of topics, ranging from mechanistically driven basic science research to randomized controlled trials. While basic science research is slow to impact clinical care, transformational changes in a field occur through basic investigations. On the other hand, clinical research yields incremental changes to clinical care. Basic research intends to change understanding whereas clinical research intends to change practice. However, the best approach is to incorporate both basic and clinical research into a translational program which makes new discoveries and effects positive changes to clinical practice. This review examines current research in FPD, with focus on translational potential, and ponders the future of FPD research. With a goal of improving the care and outcomes in patients with FPD, a strategic collaboration of stakeholders (patients, advocacy groups, physicians, researchers, professional medical associations, legislators, governmental biomedical research agencies, pharmaceutical companies, and medical device companies) is an absolute requirement in order to generate funding needed for FPD translational research.

Acupuncture for the treatment of vulvodynia: a randomized wait-list controlled pilot study.
Schlaeger JM, Xu N, Mejta CL, Park CG, Wilkie DJ.
J Sex Med. 2015 Apr;12(4):1019-27. doi: 10.1111/jsm.12830. Epub 2015 Jan 30.
http://www.ncbi.nlm.nih.gov/pubmed/25639289

INTRODUCTION: The incidence of vulvodynia in American women has been reported to be between 8.3% and 16%. However, there is no consistently effective standardized treatment for vulvodynia. **AIM:** To determine the feasibility and potential effects of using a standardized acupuncture protocol for the treatment of women with vulvodynia. **MAIN OUTCOME MEASURES:** The primary outcome was vulvar pain, and sexual function was the secondary outcome. Pain was assessed by the Short-Form McGill Pain Questionnaire, and function was measured by the Female Sexual Function Index (FSFI). **METHODS:** Thirty-six women with vulvodynia met inclusion criteria. The women were randomly assigned either to the acupuncture group or to the wait-list control group. The 18 subjects assigned to the acupuncture group received acupuncture two times per week for 5 weeks for a total of 10 sessions. **RESULTS:** Reports of vulvar pain and dyspareunia were significantly reduced, whereas changes in the aggregate FSFI scores suggest significant improvement in sexual functioning in those receiving acupuncture vs. those who did not. Acupuncture did not significantly increase sexual desire, sexual arousal, lubrication, ability to orgasm or sexual satisfaction in women with vulvodynia. **CONCLUSION:** This was the first randomized controlled pilot study to examine the use of acupuncture for the treatment of vulvodynia. The acupuncture protocol was feasible and in this small sample appeared to reduce vulvar pain and dyspareunia with an increase in overall sexual function for women with vulvodynia. This study should be replicated in a larger double-blinded randomized controlled trial

Women in "Sexual" Pain: Exploring the Manifestations of Vulvodynia.
Dargie E, Pukall CF.
J Sex Marital Ther. 2015 Apr 7:1-15.
http://www.ncbi.nlm.nih.gov/pubmed/25849434

This study explored the sexual and pain histories and pain presentations of women with forms of chronic vulvar pain (i.e., vulvodynia). One hundred and seventy-seven women with five subtypes of vulvodynia completed an online questionnaire. Groups were similar across several domains: participants experienced pain for many years during sexual and nonsexual activities, and pain was rated as moderate to severe. However, several differences emerged when considering pain development, number of sexual partners, and treatment seeking. This study illustrates how severe vulvodynia pain can be, regardless of subtype. However, not all vulvodynia sufferers are alike, and distinctions between research and clinical practice are highlighted.

Mast cell infiltrates in vulvodynia represent secondary and idiopathic mast cell hyperplasias.
Regauer S, Eberz B, Beham-Schmid C.
APMIS. 2015 May;123(5):452-6. doi: 10.1111/apm.12372.
http://www.ncbi.nlm.nih.gov/pubmed/25912132

Mast cell infiltrates in tissues of vulvodynia are common, but they have not been characterized for criteria of neoplastic mast cell disease or correlated with patient's concomitant diseases associated with increased mast cells. Formalin-fixed specimens of 35 patients with vulvodynia were evaluated immunohistochemically with antibodies to CD 3,4,8,20,117c and human mast cell tryptase, and for

WHO-criteria of neoplastic mastocytosis (>25% spindled mast cell, CD25 expression, point mutations of the c-kit gene (D816V), and chronically elevated serum tryptase levels). Only 20/35 specimens showed a T-lymphocyte dominant inflammatory infiltrate on HE-stained sections, but all showed mast cells. 4/35 biopsies showed <10 mast cells/mm(2) , 15/35 specimens 40-60 mast cells/mm(2) and 16/35 specimens >60 mast cells/mm(2) (average 80/mm(2)). Control tissue contained typically <10 mast cells/mm(2) . Spindling, CD25-expression, c-kit gene mutations, or increased serum tryptase levels were not detected. 26/35 (74%) patients had concomitant autoimmune diseases, psoriasis, atopy, various allergies, preceding infections. Independent of the subtype of vulvodynia, the majority of mast cell rich biopsies with >40 mast cells/mm(2) were classified as a secondary mast cell disorder reflecting an activated immune system in 75% of vulvodynia patients. Patients with increased mast cells may benefit from medical therapy targeting mast cells.

Vulvar vestibulodynia: strategies to meet the challenge.
Bonham A.
Obstet Gynecol Surv. 2015 Apr;70(4):274-8. doi: 10.1097/OGX.0000000000000169.
http://www.ncbi.nlm.nih.gov/pubmed/25900527

Vulvodynia is a condition that affects approximately 8% to 12% of women during their lifetimes. Vulvar vestibulodynia (VVD), the most common form of this condition, is characterized by pain with touch at the vulvar vestibule and resulting entryway dyspareunia. Studies suggest a multifactorial etiology; hormonal effects, muscle dysfunction, personality, psychosocial factors, and inflammatory mediators may all play some role in the development of this condition. Both peripheral and central sensitization to pain have been implicated in the development of enhanced pain experienced by women with VVD. Recommendations for the treatment of this condition exist; however, treatments of this condition have not been well studied. Few prospective placebo-controlled trials exist, and many of those that do have failed to show clinically relevant efficacy associated with traditional therapies. New studies into the etiology of this condition, as well as potential new therapies, are emerging, but the optimal approach has yet to be defined. Proper vulvar hygiene is recommended, and traditional therapies such as topical medications and centrally acting oral medications may continue to play a role in treatment. Newer studies elucidating the effects of personality and cognitive factors as well as pelvic floor muscle dysfunction in the development of this condition lend support for the inclusion of cognitive behavioral therapy and physical therapy/surface electromyographic biofeedback in the treatment regimen. Surgery for this condition exists, with success rates of 60% to 90%; however, it is recommended only in cases that have failed to respond to traditional therapy.

Milnacipran in provoked vestibulodynia: efficacy and predictors of treatment success.
Brown C, Bachmann G, Foster D, Rawlinson L, Wan J, Ling F.
J Low Genit Tract Dis. 2015 Apr;19(2):140-4.
http://www.ncbi.nlm.nih.gov/pubmed/25089551

OBJECTIVE: This study aimed to collect preliminary evidence on the efficacy of milnacipran in reducing pain in women with provoked vestibulodynia (PVD) and to identify which patient characteristics predict treatment success. **MATERIALS AND METHODS:** A 12-week open-label trial was conducted in 22 women with PVD. The Pain Rating Index of the McGill Pain Questionnaire was the primary outcome measure. Other outcome measures included daily diaries, Beck Depression Inventory, State-Trait Anxiety Inventory, Female Sexual Function Index, Brief Pain Inventory, a personal or family history of

fibromyalgia, and PVD subtype. **RESULTS:** Milnacipran (50-200 mg/d) significantly reduced pain severity on the Pain Rating Index ($p = .001$), coital pain ($p = .001$), tampon pain ($p = .003$), and mean vulvar pain ($p \leq .001$). Scores were also decreased on the Beck Depression Inventory ($p = .015$), State-Trait Anxiety Inventory ($p = .046$), and Brief Pain Inventory ($p = .019$) and increased on the Female Sexual Function Index ($p = .004$). Fibromyalgia history, PVD subtype, presence of depression or anxiety, and level of impairment did not affect treatment response. By logistic regression analysis, it was noted that the odds of treatment success was 3 times higher among women who, at pretreatment, had a sexually satisfying relationship compared to those who did not (odds ratio = 3.30, confidence interval = 1.04-10.50, $p = .043$). **CONCLUSIONS:** Milnacipran significantly reduced vestibular pain in women with PVD. Treatment success was predicted by pretreatment sexual satisfaction. A larger randomized controlled trial is necessary to confirm the efficacy of milnacipran in PVD and to identify other possible predictors of treatment outcome.

The Use of Specific Myofascial Release Techniques by a Physical Therapist to Treat Clitoral Phimosis and Dyspareunia

Pamela Morrison, Susan Kellogg Spadt, Andrew Goldstein

DOI: 10.1097/JWH.0000000000000023
http://www.pamelamorrisonpt.com/pmblog/the-use-of-specific-myofascial-release-techniques-by-a-physical-therapist-to-treat-clitoral-phimosis-and-dyspareunia/
Journal of Women's Health Physical Therapy
January/April 2015
Vol. 39 - Issue 1: p 17–28

Introduction: Clitoral phimosis is adherence of the clitoral prepuce to the glans and can result from inflammatory dermatoses, blunt trauma, chronic infection, and inadequate hygiene. **Aim:** The aim of this report was to demonstrate myofascial release (MFR) techniques utilized by a physical therapist to treat clitoral phimosis. **Methods:** The patient was a 41-year-old woman with low back pain, a bruised sensation of her pubic region, vulvar pain provoked by sexual arousal, decreased clitoral sensitivity, dyspareunia, and anorgasmia. The patient sustained a blunt trauma injury to the vulva. Examination revealed lumbosacral and pelvic dysfunction, pelvic floor muscle dysfunction, bone bruise of the pubic bone, and decreased retractability of the clitoral prepuce and scarring. Eleven physical therapy sessions over 16 weeks included stretching, joint mobilization, muscle energy techniques, transvaginal pelvic floor muscle massage, clitoral prepuce MFR techniques, biofeedback, Integrative Manual Therapy (IMT) techniques, nerve mobilization, and therapeutic and motor control exercises. The patient applied topical clobetasol 0.05% cream for 30 days. **Results:** The low back pain was reduced and full resolution of her vulvar pain, dyspareunia, and pubic bone bruised sensation resulted. Mobility of the clitoral prepuce was restored. Normal clitoral sensitivity and clitoral orgasm returned. Symptom resolution was confirmed upon telephone evaluation at 6 months. **Conclusion:** With proper training, physical therapists managing patients with dyspareunia can identify clitoral phimosis and use specifi c MFR as a conservative treatment approach. Physical therapy techniques can be performed alone or in concert with medical therapy.

Activation of vestibule-associated lymphoid tissue in localized provoked vulvodynia.
Tommola P, Bützow R, Unkila-Kallio L, Paavonen J, Meri S.
Am J Obstet Gynecol. 2015 Apr;212(4):476.e1-8. doi: 10.1016/j.ajog.2014.10.1098. Epub 2014 Oct 30.
http://www.ncbi.nlm.nih.gov/pubmed/25448516

OBJECTIVE: Localized provoked vulvodynia (LPV) may have inflammatory etiology. We wanted to find out whether the cell-mediated immune system becomes activated in the vestibular mucosa in LPV. **STUDY DESIGN:** This was a controlled cross-sectional study. Vestibular mucosal specimens were obtained from 27 patients with severe LPV and 15 controls. Detailed clinical history of the patients was obtained. For immunohistochemistry, antibodies against CD3 (T cells), CD20 (B cells), IgA (mucosal plasma cells), CD163 (dendritic cells [DCs]), CD68 (macrophages), and CD117 (mast cells) were employed. Mann-Whitney U test and $\chi(2)$ test were used for statistical analyses. **RESULTS:** More B lymphocytes and mature mucosal IgA-plasma cells were found in patients than in controls ($P < .001$ and $P < .001$, respectively). In LPV samples, B and T cells were arranged into germinal centers representing local immune activation. Germinal centers were not seen in controls. Antigen-presenting DCs and macrophages were found both in patients and controls with similar densities. DCs were found to extend their dendrites into the luminal space through an intact epithelium. Similar amounts of mast cells were found evenly scattered throughout the stroma of vestibular mucosa of both patients and controls. **CONCLUSION:** We demonstrate here local organized vestibule-associated lymphoid tissue analogous to mucosa-associated lymphoid tissue. Vestibule-associated lymphoid tissue may emerge as a response to local infection or inflammation in LPV.

Comorbid Disorders

Botulinum toxin in urology: a review of clinical potential in the treatment of urologic and sexual conditions.
Chung E.
Expert Opin Biol Ther. 2015 Jan;15(1):95-102. doi: 10.1517/14712598.2015.974543. Epub 2014 Oct 27.
http://www.ncbi.nlm.nih.gov/pubmed/25347039

INTRODUCTION: In recent years, there has been an increased interest in the use of botulinum neurotoxin (BoNT) to treat medical conditions refractory to conventional treatment. The following article provides an overview of the clinical use and efficacy of BoNT in the treatment of various urologic and sexual conditions. **AREAS COVERED:** BoNT has been accepted and/or explored as novel treatment for various lower urinary tract and sexual dysfunctions such as overactive bladder/detrusor overactivity (DO), detrusor-sphincter dyssynergia (DSD), benign prostatic hyperplasia, interstitial cystitis/painful bladder syndrome, chronic pelvic pain and more recently premature ejaculation. The following terms 'botulinum toxin', 'BoNT', 'botulinum toxin A', 'Botox', 'Dysport', 'Xeomin', 'botulinum toxin B', 'Myobloc', 'OnabotulinumA', 'RimabotulinumA', 'IncobotulinumA' and 'AbobotulinumA' were used to search several databases including MEDLINE, Pubmed, EMBASE, CINAHL and clinicaltrials.gov for inclusion in this review article. Only English language articles were considered and all studies were limited to BoNT therapy in urological conditions in the adult population. **EXPERT OPINION:** BoNT-A has received regulatory approval for use in neurogenic DO and overactive bladder, but its use remains unlicensed in other lower urinary tract conditions such as non-neurogenic lower urinary tract symptoms in men with benign prostatic hyperplasia, bladder pain syndrome and DSD. Published literature shows that BoNT can be effective in carefully selected patient groups, has minimal adverse event profile and is

generally well tolerated by many patients. However, many questions remain unanswered and larger scale multi-institutional studies are required to determine the key factors in BoNT treatment success.

A new paradigm in chronic bladder pain.
Wesselmann U.
J Pain Palliat Care Pharmacother. 2014 Dec;28(4):406-8. doi: 10.3109/15360288.2014.972006. Epub 2014 Oct 28.
http://www.ncbi.nlm.nih.gov/pubmed/25348226

The concept of visceral pain has moved from organ-centered disease to a conceptualization based on pathophysiological mechanisms, integrating psychosocial and sexual dimensions. The terms painful bladder syndrome and bladder pain syndrome have been coined to include all patients with bladder pain. There is substantial overlap between IC/BPS and other pelvic/abdominal pain syndromes IC/BPS is likely to be underdiagnosed and undertreated in both men and women IC/BPS requires a multidisciplinary team approach toward management.

A pilot randomized trial of levator injections versus physical therapy for treatment of pelvic floor myalgia and sexual pain.
Zoorob D, South M, Karram M, Sroga J, Maxwell R, Shah A, Whiteside J.
Int Urogynecol J. 2014 Dec 20.
http://www.ncbi.nlm.nih.gov/pubmed/25527482

INTRODUCTION AND HYPOTHESIS: Our aim was to determine the effects of pelvic floor physical therapy (PT) and levator-directed trigger-point injections (LTPI) on sexual function and levator-related pelvic pain. STUDY DESIGN: A randomized trial among women with pelvic floor myalgia (PFM) was performed wherein participants received either PT or LTPI. Pain was assessed and 1 month posttreatment completion. Levator-based pain was assessed using a numeric rating scale (NRS) and the Patient Global Impression of Improvement (PGI-I) scale. Sexual function was assessed using the Female Sexual Function Index (FSFI). RESULTS: Twenty-nine women completed the study (17 had PT, 12 had LTPI). Both groups reported reduction in vaginal pain: mean NRS change from baseline of 4.47 [standard deviation (SD) 2.12) for PT and 4.67 (SD 1.72) for LTPI ($p = 0.8$)]. A >50 % improvement in NRS was documented among 59 % of women receiving PT and 58 % receiving LTPI ($p = 1.0$). Consistent with NRS scores, mean PGI-I score was 2.50 (SD 1.17) for PT and 2.17 (SD 1.01) for LTPI ($p = 0.5$). Mean change in FSFI favored PT [PT +8.87 (SD 5.60), LTPI +4.00 (SD 5.24), $p = 0.04$], reflecting improvement in the sexual pain domain favoring PT ($p = 0.02$). However, the time in weeks to effect improvement favored LTPI if controlling for the degree of change in NRS ($p = 0.01$) and FSFI ($p = 0.01$). CONCLUSIONS: Vaginal myalgia and sex-related pain improved with pelvic floor PT and LTPI. Time-to-effect improvement and significance of therapy are dependent on treatment type.

Disease-related differences in resting-state networks: a comparison between localized provoked vulvodynia, irritable bowel syndrome, and healthy control subjects.
Gupta A, Rapkin AJ, Gill Z, Kilpatrick L, Fling C, Stains J, Masghati S, Tillisch K, Mayer EA, Labus JS.
Pain. 2015 May;156(5):809-19. doi: 10.1097/01.j.pain.0000461289.65571.54.
http://www.ncbi.nlm.nih.gov/pubmed/25735001

Localized provoked vulvodynia (LPVD) affects approximately 16% of the female population, but biological mechanisms underlying symptoms remain unknown. Like in other often comorbid chronic pain disorders, altered sensory processing and modulation of pain, including central sensitization, dysregulation of endogenous pain modulatory systems, and attentional enhancement of pain perception, have been implicated. The aim of this study was to test whether regions of interest showing differences in LPVD compared to healthy control subjects (HCs) in structural and evoked-pain neuroimaging studies, also show alterations during rest when compared with HCs and a chronic pain control group (irritable bowel syndrome [IBS]). Functional magnetic resonance imaging was performed during resting state in 87 age-matched premenopausal females (29 LPVD, 29 HCs, and 29 IBS). Group-independent component analysis and general linear models were applied to investigate group differences in the intrinsic connectivity of regions comprising sensorimotor, salience, and default mode resting-state networks. Subjects with LPVD showed substantial alterations in the intrinsic connectivity of these networks compared with HCs and IBS. The intrinsic connectivity of many of the regions showing group differences during rest were moderately associated with clinical symptom reports in LPVD. Findings were robust to controlling for affect and medication usage. The current findings indicate that subjects with LPVD have alterations in the intrinsic connectivity of regions comprising the sensorimotor, salience, and default mode networks. Although shared brain mechanisms between different chronic pain disorders have been postulated, the current findings suggest that some alterations in functional connectivity may show disease specificity.

Botulinum Toxin A Injections Into Pelvic Floor Muscles Under Electromyographic Guidance for Women With Refractory High-Tone Pelvic Floor Dysfunction: A 6-Month Prospective Pilot Study.
Morrissey D, El-Khawand D, Ginzburg N, Wehbe S, O'Hare P 3rd, Whitmore K.
Female Pelvic Med Reconstr Surg. 2015 Mar 18.
http://www.ncbi.nlm.nih.gov/pubmed/25900057

OBJECTIVES: High-tone pelvic floor dysfunction (HTPFD) is a debilitating chronic pain disorder for many women with significant impact on their quality of life (QoL). Our objective was to determine the efficacy of electromyography-guided onabotulinumtoxinA (Botox; Allergan, Irvine, Calif) injections in treating patient's perception of pelvic pain and improving QoL measurement scores. **METHODS:** This is a prospective pilot open-label study of women with chronic pelvic pain and HTPFD who have failed conventional therapy between January 2011 and August 2013. Botox injections (up to 300 U) were done using needle electromyography guidance, from a transperineal approach, to localize spastic pelvic floor muscles (PFMs). Data were collected at baseline, 4, 8, 12, and 24 weeks after injections. This included demographics; Visual Analog Scale (VAS) scores for pain and dyspareunia; validated questionnaires for symptoms, QoL, and sexual function; Global Response Assessment scale for pelvic pain; digital examination of PFM for tone and tenderness; and vaginal manometry. Side effects were also recorded. **RESULTS:** Out of 28 women who enrolled in the study, 21 completed the 6-month follow-up and qualified for analysis. The mean (SD) age was 35.1 (9.4) years (range, 22-50 years), and the mean (SD) body mass index was 25 (4.4). Comorbidities included interstitial cystitis/bladder pain syndrome (42.9%) and vulvodynia (66.7%). Overall, 61.9% of subjects reported improvement on Global Response

Assessment at 4 weeks and 80.9% at 8, 12, and 24 weeks post injection, compared with baseline. Of the subjects who were sexually active at baseline, 58.8% (10/17), 68.8% (11/16), 80% (12/15), and 83.3% (15/18) reported less dyspareunia at 4, 8, 12, and 24 weeks, respectively. Dyspareunia Visual Analog Scale score significantly improved at weeks 12 (5.6, P = 0.011) and 24 (5.4, P = 0.004) compared with baseline (7.8). Two of the 4 patients who avoided sexual activity at baseline secondary to dyspareunia resumed and tolerated intercourse after Botox. Sexual dysfunction as measured by the Female Sexual Distress Scale significantly improved at 8 weeks (27.6, P = 0.005), 12 weeks (27.9, P = 0.006), and 24 weeks (22.6, P < 0.001) compared with baseline (34.5). The Short-Form 12 Health Survey (SF-12) showed improved QoL in the physical composite score at all post injections visits (42.9, 44, 43.1, and 45.5 vs 40 at baseline; P < 0.05), and in the mental composite score at both 12 and 24 weeks (44.3 and 47.8 vs 38.5, P = 0.012). Vaginal manometry demonstrated significant decrease in resting pressures and in maximum contraction pressures at all follow-up visits (P < 0.05). Digital assessment of PFM (on a scale from 0 to 4) showed decreased tenderness on all visits (mean of 1.9, 1.7, 1.8, 1.9; P < 0.001) compared with baseline (2.8). Reported postinjection adverse effects included worsening of the following preexisting conditions: constipation (28.6%), stress urinary incontinence (4.8%), fecal incontinence (4.8%), and new onset stress urinary incontinence (4.8%). **CONCLUSIONS:** Electromyography-guided Botox injection into PFM could be beneficial for women with refractory HTPFD who have failed conservative therapy.

Central and Peripheral Pain Generators in Women with Chronic Pelvic Pain: Patient Centered Assessment and Treatment.

Hoffman D.

Curr Rheumatol Rev. 2015;11(2):146-66.
http://www.ncbi.nlm.nih.gov/pubmed/26088216

Women with chronic pelvic pain (CPP) often present without obvious cause on imaging studies, laboratory values or physical exam. Dysfunctional sensory processing in the central nervous system (CNS) may explain pain of unclear origin. Central sensitization (CS), a mechanism of centrally mediated pain, describes this abnormal processing of sensory information. Women with CPP often present with several seemingly unrelated symptoms. This can be explained by co-existing chronic pain syndromes occurring in the same patient. Central sensitization occurs in all of these pain syndromes, also described as dysfunctional pain syndromes, and thus may explain why several often occur in the same patient. Six of the most common pain disorders that co-exist in CPP include endometriosis, painful bladder syndrome/interstitial cysitis, vulvodynia, myofascial pain/ pelvic floor hypertonus, irritable bowel syndrome, and primary dysmenorrhea. Central pain generators, (pain originating from CS) and peripheral pain generators, (pain from local tissue damage), can both occur in each of these six conditions. These pain generators will be described. Chronic pain, specifically dysfunctional sensory processing, is recognized as a systemic disease process like diabetes to be managed as opposed to a local problem to be "fixed" or cured. A multi-disciplinary approach to assessment and treatment with a focus on improving emotional, physical and social functioning instead of focusing strictly on pain reduction is more effective in decreasing disability. This is best achieved by determining the patient's needs and perspective through a patient-centered approach. Algorithms for such an approach to assessment and treatment are outlined.

New concepts on functional chronic pelvic and perineal pain: pathophysiology and multidisciplinary management.
Ploteau S, Labat JJ, Riant T, Levesque A, Robert R, Nizard J.
Discov Med. 2015 Mar;19(104):185-92.
http://www.ncbi.nlm.nih.gov/pubmed/25828522

The management of chronic pelvic and perineal pain has been improved by a better understanding of the mechanisms of this pain and an optimized integrated multidisciplinary approach to the patient. The concept of organic lesions responsible for a persistent nociceptive factor has gradually been replaced by that of dysregulation of nociceptive messages derived from the pelvis and perineum. In this setting, painful diseases identified by organ specialists are usually also involved and share several common denominators (triggering factors, predisposing clinical context). These diseases include painful bladder syndrome, irritable bowel syndrome, vulvodynia, and chronic pelvic pain syndrome. The painful symptoms vary from one individual to another and according to his or her capacity to activate pain inhibition/control processes. Although the patient often attributes chronic pain to a particular organ (with the corollary that pain will persist until the organ has been treated), this pain is generally no longer derived from the organ but is expressed via this organ. Several types of clinical presentation of complex pelvic pain have therefore been pragmatically identified to facilitate the management of treatment failures resulting from a purely organ-based approach, which can also reinforce the patient's impression of incurability. These subtypes correspond to neuropathic pain, central sensitization (fibromyalgia), complex regional pain syndrome, and emotional components similar to those observed in post-traumatic stress disorder. These various components are also often associated and self-perpetuating. Consequently, when pelvic pain cannot be explained by an organ disease, this model, using each of these four components associated with their specific mechanisms, can be used to propose personalized treatment options and also to identify patients at high risk of postoperative pelvic pain (multi-operated patients, central sensitization, post-traumatic stress disorder, etc.), which constitutes a major challenge for prevention of these types of pain that have major implications for patients and society.

Relationship between female pelvic floor dysfunction and sexual dysfunction: an observational study.
Bortolami A, Vanti C, Banchelli F, Guccione AA, Pillastrini P.
J Sex Med. 2015 May;12(5):1233-41. doi: 10.1111/jsm.12882. Epub 2015 Apr 8.
http://www.ncbi.nlm.nih.gov/pubmed/25855126

INTRODUCTION: The ability to express one's sexuality and engage in sexual activity requires multisystemic coordination involving many psychological functions as well as the integrity of the nervous, hormonal, vascular, immune, and neuromuscular body structures and functions. **AIM:** The purpose of this study was to investigate the associations among pelvic floor function, sexual function, and demographic and clinical characteristics in a population of women initiating physical therapy evaluation and treatment for pelvic floor-related dysfunctions (urinary incontinence, pelvic organ prolapse, vulvodynia, vaginismus, and constipation). **METHODS:** We consented and collected completed demographic data and data related to symptoms and clinical condition on 85 consecutive patients in an outpatient physical therapy clinic. Clinical and anthropometric characteristics were analyzed descriptively. Analysis of variance and linear regression analyses were used to analyze Female Sexual Function Index (FSFI) scale ratings, whereas zero-inflated beta-binomial regression was applied to the pain subscale. **MAIN OUTCOME MEASURES:** Main outcome measure was FSFI score, whereas the secondary outcome measure was the FSFI subscale score related to pain. **RESULTS:** Women in our sample were 38 years old on average, 33% of whom had given birth and 82% of whom had high tone

pelvic floor. Being in the middle-tercile age group and exhibiting low pelvic floor tone (Beta = 6.8; 95% confidence interval [CI] = [1.4; 12.0]) were significantly associated with lower levels of sexual dysfunction. Women with low tone pelvic floor also reported lower pain (odds ratio = 4.0; 95% CI = [1.6; 9.6]), whereas younger aged and physically unsatisfied subjects were more likely not to have sexual activity in the month prior to scale measurement. **CONCLUSION:** In female patients with pelvic floor muscle dysfunction undergoing physical therapy and rehabilitation, sexual dysfunction appears to be significantly correlated with age and high pelvic floor muscle tone.

Dermatological Disorders/Infectious Disease

Safety and Efficacy of Human Fibroblast Lysate Cream for Vulvar Lichen Sclerosus: A Randomized Placebo-Controlled Trial.
Goldstein AT, Burrows LJ, Belkin ZR, Pfau R, Bremmer M, Goldfinger C, Dreher F.
Acta Derm Venereol. 2015 Jan 29. doi: 10.2340/00015555-2052.
http://www.ncbi.nlm.nih.gov/pubmed/25634582

Abstract is missing.

Conscious sedation with inhaled 50% nitrous oxide/oxygen premix in photodynamic therapy sessions for vulvar lichen sclerosus treatment.
Cabete J, Campos S, Lestre S.
An Bras Dermatol. 2015 Jan-Feb;90(1):120-2. doi: 10.1590/abd1806-4841.20153112.
http://www.ncbi.nlm.nih.gov/pubmed/25672311

Photodynamic therapy has been described as an effective therapeutic option in selected cases of anogenital lichen sclerosus that are refractory to first-line treatments. However, procedure-related pain is a limiting factor in patient adherence to treatment. The authors report the case of a 75-year-old woman with highly symptomatic vulvar lichen sclerosus, successfully treated with photodynamic therapy. An inhaled 50% nitrous oxide/oxygen premix was administered during sessions, producing a pain-relieving, anxiolytic, and sedative effect without loss of consciousness. This ready-to-use gas mixture may be a well-tolerated and accepted alternative to classical anesthetics in Photodynamic therapy, facilitating patients' adherence to illumination of pain-prone areas.

Humoral immune responses to Candida albicans complement receptor 3-related protein in the atopic subjects with vulvovaginal candidiasis. Novel sensitive marker for Candida infection.
Paulovičová E, Bujdáková H, Chupáčová J, Paulovičová L, Kertys P, Hrubiško M.
FEMS Yeast Res. 2015 Feb;15(2). pii: fou001. doi: 10.1093/femsyr/fou001.
http://www.ncbi.nlm.nih.gov/pubmed/25673750

In vitro evaluation of specific anti-Candida albicans sera antibodies based on synthetically prepared complement receptor 3-related protein (CR3-RP) mimicking the structure of native complement receptor 3 in a cohort of 72 patients with atopy and recurrent Candida vulvovaginitis (RVC) revealed effective humoral response against Candida CR3-RP. The most significant have been IgM and IgA isotype antibodies (33 and 47% positive cases, respectively). The quantitative evaluation of anti-CR3RP isotype

antibodies was confronted with results of commercial ELISA anti-C. albicans antibodies diagnostics based on C. albicans cell wall mannan and β-glucan antigens, the most significant correlation being observed with anti-CR3-RP IgM and anti-β-D-glucan IgM (r(2) = 0.624) followed by isotype IgA (r(2) = 0.381). The immunogenicity and immunoreactivity of CR3RP antigen in RVC patients' sera had been evaluated with regard to the results reached by counterimmunoelectrophoresis and heterogeneous enzyme immunoassay. Obviously, synthetically prepared CR3-RP mimicking the Candida cell-wall-derived structure moiety represents a promising immunological tool not only for Candida serodiagnostics, but also prospectively for follow-up of targeted antifungal therapy and as promising Candida vaccine candidate.

Neutrophil Gelatinase-Associated Lipocalin Concentration in Vaginal Fluid: Relation to Bacterial Vaginosis and Vulvovaginal Candidiasis.

Beghini J, Giraldo PC, Linhares IM, Ledger WJ, Witkin SS.

Reprod Sci. 2015 Feb 10. pii: 1933719115570914.

http://www.ncbi.nlm.nih.gov/pubmed/25670719

OBJECTIVE: Neutrophil gelatinase-associated lipocalin (NGAL) is a component of innate immunity that prevents iron uptake by microorganisms. We evaluated whether NGAL was present in vaginal fluid and whether concentrations were altered in women with bacterial vaginosis (BV) or vulvovaginal candidiasis (VVC). **METHODS:** Vaginal secretions from 52 women with VVC, 43 with BV, and 77 healthy controls were assayed by enzyme-linked immunosorbent assay for NGAL and for concentrations of l-lactic acid. **RESULTS:** The median concentration of NGAL in vaginal fluid was significantly higher in control women (561 pg/mL) than in women with BV (402 pg/mL; P = .0116) and lower in women with VVC (741 pg/mL; P = .0017). Median lactic acid levels were similar in controls (0.11 mmol/L) and women with VVC (0.13 mmol/L) and were lower in women with BV (0.02 mmol/L; P< .0001). The NGAL and lactic acid concentrations were highly correlated (P < .0001). **CONCLUSION:** A decrease in Lactobacilli and/or lactic acid plus the absence of leukocytes results in lower vaginal NGAL levels that might facilitate the growth of bacteria associated with BV.

Site-specific mesenchymal control of inflammatory pain to yeast challenge in vulvodynia-afflicted and pain-free women.

Foster DC, Falsetta ML, Woeller CF, Pollock SJ, Song K, Bonham A, Haidaris CG, Stodgell CJ, Messing SP, Iadarola M, Phipps RP.

Pain. 2015 Mar;156(3):386-96. doi: 10.1097/01.j.pain.0000460320.95267.5d.

http://www.ncbi.nlm.nih.gov/pubmed/25679469

Fibroblast strains were derived from 2 regions of the lower genital tract of localized provoked vulvodynia (LPV) cases and pain-free controls. Sixteen strains were derived from 4 cases and 4 controls, age and race matched, after presampling mechanical pain threshold assessments. Strains were challenged with 6 separate stimuli: live yeast species (Candida albicans, Candida glabrata, Candida tropicalis, and Saccharomyces cerevisiae), yeast extract (zymosan), or inactive vehicle. Production of prostaglandin E2 (PGE2) and interleukin 6 (IL-6) were proinflammatory response measures. Highest IL-6 and PGE2 occurred with vestibular strains after C albicans, C glabrata, and zymosan challenges, resulting in the ability to significantly predict IL-6 and PGE2 production by genital tract location. After C albicans and C glabrata challenge of all 16 fibroblast strains, adjusting for dual sampling of subjects, PGE2 and IL-6 production significantly predicted the presampling pain threshold from the genital tract site of

sampling. At the same location of pain assessment and fibroblast sampling, in situ immunohistochemical (IHC)(+) fibroblasts for IL-6 and Cox-2 were quantified microscopically. The correlation between IL-6 production and IL-6 IHC(+) was statistically significant; however, biological significance is unknown because of the small number of IHC(+) IL-6 fibroblasts identified. A low fibroblast IL-6 IHC(+) count may result from most IL-6 produced by fibroblasts existing in a secreted extracellular state. Enhanced, site-specific, innate immune responsiveness to yeast pathogens by fibroblasts may be an early step in LPV pathogenesis. Fibroblast strain testing may offer an attractive and objective marker of LPV pathology in women with vulvodynia of inflammatory origin.

Diverse Nitrogen Sources in Seminal Fluid Act in Synergy to Induce Filamentous Growth of Candida albicans.

Alvarez FJ, Ryman K, Hooijmaijers C, Bulone V, Ljungdahl PO.

Appl Environ Microbiol. 2015 Feb 6. pii: AEM.03595-14.

http://www.ncbi.nlm.nih.gov/pubmed/25662979

The pathogenic fungus Candida albicans is the leading cause of vulvovaginal candidiasis (VVC). VVC represents a major quality-of-life issue for women during their reproductive years, a stage of life where the vaginal epithelium is subject to periodic hormonal induced changes associated with menstruation and concomitant exposure to serum, and potential intermittent contact with seminal fluid. Seminal fluid potently triggers Candida albicans to switch from yeast-like to filamentous modes of growth, a developmental response tightly linked to virulence. Conversely, vaginal fluid inhibits filamentation. Here, we used artificial formulations of seminal (ASF) and vaginal (AVF) fluids that faithfully mimic the genuine fluids to assess the contribution of the individual components within these fluids to affect filamentation. The high levels of albumin, amino acids and N-acetylglucosamine in seminal fluid act synergistically as potent inducers of filamentous growth, even at atmospheric levels of CO_2 and reduced temperatures (30 °C). Using a simplified in vitro model that mimics the natural introduction of seminal fluid into the vulvovaginal environment, a pulse of ASF was found to exert an enduring potential to overcome the inhibitory efficacy of AVF on filamentation. These findings suggest that a transient but substantial change in the nutrient levels within the vulvovaginal environment during unprotected coitus can induce resident C. albicans cells to engage developmental programs associated with virulent growth.

Vulvar dermatoses: a histopathologic review and classification of 183 cases.

Chan MP, Zimarowski MJ.

J Cutan Pathol. 2015 May 21. doi: 10.1111/cup.12541.

http://www.ncbi.nlm.nih.gov/pubmed/25996085

BACKGROUND: Vulvar dermatoses are often difficult to classify due to histopathologic overlap. We aimed to report our experience at a single institution. **METHODS:** A total of 183 non-neoplastic, non-infectious vulvar biopsies were reviewed. Associations between histopathologic features and specific diagnoses were analyzed by Chi-squared tests. **RESULTS:** Twenty-two biopsies (12.0%) showed two concurrent processes. A limited differential rather than a definitive diagnosis was rendered in 15 cases (8.2%). The final diagnoses included lichen sclerosus (LS) (38.8%), lichen simplex chronicus (LSC) (29.0%), eczematous dermatitis (23.0%), Zoon vulvitis (8.2%), non-specific/resolved dermatitis (5.5%), hidradenitis suppurativa (2.7%), Behçet disease (2.2%), lichen planus (1.6%), ruptured cyst (1.6%), ulcer not-otherwise-specified (1.6%), psoriasis (1.1%), radiation dermatitis (1.1%), sebopsoriasis (1.1%), seborrheic dermatitis (1.1%), epidermolytic hyperkeratosis (0.5%) and granular parakeratosis (0.5%).

Early LS and Zoon vulvitis were commonly included as part of a differential diagnosis. LS was associated with wiry collagen with lymphocyte entrapment ($p = 0.0188$). LSC was associated with zones of pale epithelium ($p = 0.0084$), and often displayed prominent fibroblasts ($p = 0.0555$). Zoon vulvitis was frequently misdiagnosed, and was associated with basal keratinocytic crowding ($p < 0.0001$). **CONCLUSIONS:** Our study has determined the relative frequencies of a wide variety of vulvar dermatoses, and identified new diagnostic clues for early LS, LSC and Zoon vulvitis.

Lichen sclerosus: a potpourri of misdiagnosed cases based on atypical clinical presentations.
Ventolini G, Patel R, Vasquez R.
Int J Womens Health. 2015 May 8;7:511-5. doi: 10.2147/IJWH.S82879. eCollection 2015.
http://www.ncbi.nlm.nih.gov/pubmed/26056492

OBJECTIVE: Lichen sclerosus (LS) is a chronic progressive inflammatory autoimmune-induced disease that primarily affects the epidermis and dermis of the external genital-anal region. Intense and recalcitrant pruritus is the hallmark of LS. Physical exam reveals thinning, hyperkeratosis, and parchment-like appearance. However, the classic symptom and signs of LS may not always be present and patients may be asymptomatic for pruritus. Hence, we describe 15 misdiagnosed cases with atypical clinical presentations. We believe that the absence of pruritus contributed to their initial misdiagnosis. The purpose of this paper is to increase awareness of atypical presentations of LS. **METHODS:** Data base review of de-identified clinical case pictures was performed. All patients had histopathology-confirmed diagnoses of LS. The data base file contains 800 cases of vulvovaginal disorders. The Institutional Review Board (IRB) considered that searching a de-identified data base of pictures did not require IRB approval. **RESULTS:** We identified 15 different atypical clinical cases. Patient ages were 18-75 years old. These patients were asymptomatic for pruritus and were misdiagnosed before they presented to the vulvovaginal specialized clinic. **CONCLUSION:** Fifteen patients asymptomatic for pruritus with histopathology-confirmed diagnosis of LS were identified. They illustrate atypical clinical presentations that LS may have.

[Vulvar pruritus: determination of the most common causes and their treatments].
[Article in Spanish]
Carrillo-Meléndrez H, Villamil-Cerda D, Espinoza-Hernández J, Lacy-Niebla RM.
Ginecol Obstet Mex. 2015 Mar;83(3):179-88.
http://www.ncbi.nlm.nih.gov/pubmed/26058171

Vulvar pruritus can be caused by a wide spectrum of diseases that depend on age, environmental and genetic factors. The most common causes are candidiasis, contact dermatitis and lichen simplex chronicus. Candidiasis is the most common cause of acute vulvar pruritus and is characterized by burning, itching and vaginal whitish secretion. Contact dermatitis is caused by irritants or allergens that are in contact with the genital area, which causes imbalance in the skin barrier causing irritation, swelling, burning, among other manifestations. Lichen simplex chronicus is characterized by lichenification (thickening of the skin) secondary to the chronic itch-scratch cycle in vulvar area. It is an illnes with a tendency to chronicity, but with topical corticosteroids treatment usually might be controlled. Prompt treatment, multidisciplinary and careful attention to irritants and secondary infections prevent these entities become an important and permanent problem.

Cellular Structural Changes in Candida albicans Caused by the Hydroalcoholic Extract from Sapindus saponaria L.

Molecules. 2015 May 22;20(5):9405-18. doi: 10.3390/molecules20059405.
http://www.ncbi.nlm.nih.gov/pubmed/26007191

Vulvovaginal candidiasis (VVC) is a disease caused by the abnormal growth of yeast-like fungi in the mucosa of the female genital tract. Candida albicans is the principal etiological agent involved in VVC, but reports have shown an increase in the prevalence of Candida non-C. albicans (CNCA) cases, which complicates VVC treatment because CNCA does not respond well to antifungal therapy. Our group has reported the in vitro antifungal activity of extracts from Sapindus saponaria L. The present study used scanning electron microscopy and transmission electron microscopy to further evaluate the antifungal activity of hydroalcoholic extract from S. saponaria (HE) against yeast obtained from VVC and structural changes induced by HE. We observed the antifungal activity of HE against 125 vaginal yeasts that belonged to four different species of the Candida genus and S. cerevisae. The results suggest that saponins that are present in HE act on the cell wall or membrane of yeast at the first moments after contact, causing damage to these structures and cell lysis.

Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis.

van Schalkwyk J, Yudin MH; Infectious Disease Committee, Yudin MH, Allen V, Bouchard C, Boucher M, Boucoiran I, Caddy S, Castillo E, Kennedy VL, Money DM, Murphy K, Ogilvie G, Paquet C, van Schalkwy JK; Society of Obstetricians and Gynaecologists of Canada.
J Obstet Gynaecol Can. 2015 Mar;37(3):266-76.
http://www.ncbi.nlm.nih.gov/pubmed/26001874

OBJECTIVE: To review the evidence and provide recommendations on screening for and management of vulvovaginal candidiasis, trichomoniasis, and bacterial vaginosis. **OUTCOMES:** OUTCOMES evaluated include the efficacy of antibiotic treatment, cure rates for simple and complicated infections, and the implications of these conditions in pregnancy. **EVIDENCE:** Published literature was retrieved through searches of MEDLINE, EMBASE, CINAHL, and The Cochrane Library in June 2013 using appropriate controlled vocabulary (e.g., vaginitis, trichomoniasis, vaginal candidiasis) and key words (bacterial vaginosis, yeast, candidiasis, trichomonas vaginalis, trichomoniasis, vaginitis, treatment). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. There were no date limits, but results were limited to English or French language materials. Searches were updated on a regular basis and incorporated in the guideline to May 2014. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, and national and international medical specialty societies. **VALUES:** The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1). Summary Statements 1. Vulvovaginal candidiasis affects 75% of women at least once. Topical and oral antifungal azole medications are equally effective. (I) 2. Recurrent vulvovaginal candidiasis is defined as 4 or more episodes per year. (II-2) 3. Trichomonas vaginalis is a common non-viral sexually transmitted infection that is best detected by antigen testing using vaginal swabs collected and evaluated by immunoassay or nucleic acid amplification test. (II-2) 4. Cure rates are equal at up to 88% for trichomoniasis treated with oral metronidazole 2 g once or 500 mg twice daily for 7 days. Partner treatment, even without screening, enhances cure rates. (I-A) 5. Current evidence of the efficacy of alternative therapies for bacterial vaginosis (probiotics, vitamin C) is limited. (I) Recommendations 1.

Following initial therapy, treatment success of recurrent vulvovaginal candidiasis is enhanced by maintenance of weekly oral fluconazole for up to 6 months. (II-2A) 2. Symptomatic vulvovaginal candidiasis treated with topical azoles may require longer courses of therapy to be resolved. (1-A) 3. Test of cure following treatment of trichomoniasis with oral metronidazole is not recommended. (I-D) 4. Higher-dose therapy may be needed for treatment-resistant cases of trichomoniasis. (I-A) 5. In pregnancy, treatment of symptomatic Trichomonas vaginalis with oral metronidazole is warranted for the prevention of preterm birth. (I-A) 6. Bacterial vaginosis should be diagnosed using either clinical (Amsel's) or laboratory (Gram stain with objective scoring system) criteria. (II-2A) 7. Symptomatic bacterial vaginosis should be treated with oral metronidazole 500 mg twice daily for 7 days. Alternatives include vaginal metronidazole gel and oral or vaginal clindamycin cream. (I-A) 8. Longer courses of therapy for bacterial vaginosis are recommended for women with documented multiple recurrences. (I-A).

Antifungal activity of clotrimazole against Candida albicans depends on carbon sources, growth phase, and morphology.

Kasper L, Miramón P, Jablonowski N, Wisgott S, Wilson D, Brunke S, Hube B.

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http://www.ncbi.nlm.nih.gov/pubmed/25976001

Vulvovaginal candidiasis (VVC), a superficial infection predominantly caused by the pathogenic fungus Candida albicans, is frequently treated with clotrimazole. Some drug formulations contain lactate for improved solubility. Lactate may modify C. albicans physiology and drug sensitivity by serving as a carbon source for the fungus and/or affecting local pH. Here we explored the effects of lactate, in combination with pH changes, on C. albicans proliferation, morphology and clotrimazole sensitivity. Moreover, we determined the influence of growth phase and morphology per se on drug sensitivity. We show that utilisation of lactate as a carbon source does not promote fast fungal proliferation or filamentation. Lactate had no influence on clotrimazole-mediated killing of C. albicans in standard fungal cultivation media but had an additive effect on the fungicidal clotrimazole action under in vitro vagina-simulative conditions. Moreover, clotrimazole-mediated killing was growth-phase and morphology dependent. Post-exponential cells were resistant to the fungicidal action of clotrimazole, while logarithmic cells were sensitive, and hyphae showed highest susceptibility. Finally, we show that treatment of preformed C. albicans hyphae with sub-lethal concentrations of clotrimazole induced a reversion to yeast phase growth. As C. albicans hyphae are considered the pathogenic morphology during mucosal infections, these data suggest that elevated fungicidal activity of clotrimazole against hyphae plus clotrimazole-induced hyphae-to-yeast reversion may help to dampen acute vaginal infections by reducing the relative proportion of hyphae and thus shifting to a non-invasive commensal-like population. In addition, lactate as an ingredient of clotrimazole formulations may potentiate clotrimazole killing of C. albicans in the vaginal microenvironment.

Persistent genital hyperinnervation following progesterone administration to adolescent female rats.
Liao Z, Smith PG.
Biol Reprod. 2014 Dec;91(6):144. doi: 10.1095/biolreprod.114.121103. Epub 2014 Oct 30.
http://www.ncbi.nlm.nih.gov/pubmed/25359899

Provoked vestibulodynia, a female pelvic pain syndrome affecting substantial numbers of women, is characterized by genital hypersensitivity and sensory hyperinnervation. Previous studies have shown that the risk of developing provoked vestibulodynia is markedly elevated following adolescent use of oral contraceptives with high progesterone content. We hypothesized that progesterone, a steroid hormone with known neurotropic properties, may alter genital innervation through direct or indirect actions. Female Sprague Dawley rats received progesterone (20 mg/kg subcutaneously) from Days 20-27; tissue was removed for analysis in some rats on Day 28, while others were ovariectomized on Day 43 and infused for 7 days with vehicle or 17beta estradiol. Progesterone resulted in overall increases in vaginal innervation at both Day 28 and 50 due to proliferation of peptidergic sensory and sympathetic (but not parasympathetic) axons. Estradiol reduced innervation in progesterone-treated and untreated groups. To assess the mechanisms of sensory hyperinnervation, we cultured dissociated dorsal root ganglion neurons and found that progesterone increases neurite outgrowth by small unmyelinated (but not myelinated) sensory neurons, it was receptor mediated, and it was nonadditive with NGF. Pretreatment of ganglion with progesterone also increased neurite outgrowth in response to vaginal target explants. However, pretreatment of vaginal target with progesterone did not improve outgrowth. We conclude that adolescent progesterone exposure may contribute to provoked vestibulodynia by eliciting persistent genital hyperinnervation via a direct effect on unmyelinated sensory nociceptor neurons and that estradiol, a well-documented therapeutic, may alleviate symptoms in part by reducing progesterone-induced sensory hyperinnervation.

Terminal innervation of female genitalia, cutaneous sensory receptors of the epithelium of the labia minora.
Schober J, Aardsma N, Mayoglou L, Pfaff D, Martín-Alguacil N.
Clin Anat. 2015 Feb 2. doi: 10.1002/ca.22502.
http://www.ncbi.nlm.nih.gov/pubmed/25644287

INTRODUCTION: Little information is available regarding the sensory nerve endings within the glabrous skin of the external female genitalia. The diversity of possible sensations suggests a variety of receptor types. Comprehensive knowledge of the sensory stimuli, including stimulus position, changes in temperature, pressure and pain, is critical for addressing pain and sexual function disorders clinically. The aim of this neuro-histological study is to document the presence and characteristics of cutaneous sensory receptors in female genital tissue. **MATERIALS AND METHODS:** Labial skin samples were obtained from ten normal girls (aged 1-9 years). The specimens were waste tissue obtained during surgical intervention. They were all obtained by the senior investigator, a pediatric urologist, after the parent or legal guardian had given informed consent. The specimens were stained by Cajal-type silver impregnation and by immunocytochemistry against protein gene product (PGP) 9.5 and neuron-specific enolase (NSE). **RESULTS:** PGP 9.5 was the most sensitive neural marker for identifying cutaneous sensory receptors. Free nerve endings (FNEs) in the papillary dermis appeared as thin fibers, varicose, branched or single processed, straight or bent. In the labia minora, FNEs were identified in the strata basale,

spinosum and granulosum of the epidermis. Non-capsulated (Meissner-like) corpuscles in the dermal papillae interdigitated with epidermal ridges of the skin. Capsulated corpuscles protruded from the deep dermis into the epidermis. Encapsulated corpuscles and cells located in the inner and outer cores were strongly positive for PGP 9.5. **CONCLUSIONS:** FNEs, Meissner's corpuscles and Pacinian corpuscles are present in the female labia minora and exhibit characteristic staining patterns.

Brain-derived neurotrophic factor as a driving force behind neuroplasticity in neuropathic and central sensitization pain: a new therapeutic target?
Nijs J, Meeus M, Versijpt J, Moens M, Bos I, Knaepen K, Meeusen R.
Expert Opin Ther Targets. 2014 Dec 18:1-12.
http://www.ncbi.nlm.nih.gov/pubmed/25519921

Introduction: Central sensitization is a form of maladaptive neuroplasticity underlying many chronic pain disorders, including neuropathic pain, fibromyalgia, whiplash, headache, chronic pelvic pain syndrome and some forms of osteoarthritis, low back pain, epicondylitis, shoulder pain and cancer pain. Brain-derived neurotrophic factor (BDNF) is a driving force behind neuroplasticity, and it is therefore crucial for neural maintenance and repair. However, BDNF also contributes to sensitization of pain pathways, making it an interesting novel therapeutic target. **Areas covered**: An overview of BDNF's sensitizing capacity at every level of the pain pathways is presented, including the peripheral nociceptors, dorsal root ganglia, spinal dorsal horn neurons, and brain descending inhibitory and facilitatory pathways. This is followed by the presentation of several potential therapeutic options, ranging from indirect influencing of BDNF levels (using exercise therapy, anti-inflammatory drugs, melatonin, repetitive transcranial magnetic stimulation) to more specific targeting of BDNF's receptors and signaling pathways (blocking the proteinase-activated receptors 2-NK-κβ signaling pathway, administration of phencyclidine for antagonizing NMDA receptors, or blockade of the adenosine A2A receptor). **Expert opinion**: This section focuses on combining pharmacotherapy with multimodal rehabilitation for balancing the deleterious and therapeutic effects of BNDF treatment in chronic pain patients, as well as accounting for the complex and biopsychosocial nature of chronic pain.

Chronic pelvic allodynia is mediated by CCL2 through mast cells in an experimental autoimmune cystitis model.
Bicer F, Altuntas CZ, Izgi K, Ozer A, Kavran M, Tuohy VK, Daneshgari F.
Am J Physiol Renal Physiol. 2015 Jan 15;308(2):F103-13. doi: 10.1152/ajprenal.00202.2014. Epub 2014 Sep 10.
http://www.ncbi.nlm.nih.gov/pubmed/25209862

The cause of chronic pelvic pain in interstitial cystitis/painful bladder syndrome (IC/PBS) remains unclear; autoimmunity is a possible etiology. We have recently shown that injection of a single immunogenic peptide of uroplakin 3A (UPK3A 65-84) induces experimental autoimmune cystitis (EAC) in female BALB/cJ mice that is unique among experimental models in accurately reflecting both the urinary symptoms and pelvic pain of IC/PBS. The aim of this project was to identify the roles of mast cells and mast cell chemoattractant/activator monocyte chemoattractant protein-1 [chemokine (C-C motif) ligand 2 (CCL2)] in the allodynia in this model. We immunized 6- to 8-wk-old female BALB/cJ mice with UPK3A 65-84 peptide and, 5-40 days later, observed increased responses to stimulation of the suprapubic abdominal and hindpaw surfaces with von Frey monofilaments compared with mice injected with adjuvant alone. Suprapubic and hindpaw tactile allodynia responses by EAC mice were blocked by

instillation of lidocaine into the bladder but not by lidocaine in the uterus, confirming the bladder as the source of the hypersensitivity. Markedly increased numbers of activated mast cells and expression of CCL2 were found in the bladder after immunization with UPK3A 65-84. Hypersensitive responses were inhibited by mast cell stabilizer cromolyn sodium and antagonists of histamine receptors 1 and 2. Furthermore, BALB/cJ mice with deletion of the Ccl2 or chemokine (C-C motif) receptor 2 gene exhibited markedly reduced allodynia and accumulation of mast cells after UPK3A 65-84 immunization. These results show that UPK3A 65-84 immunization causes chronic visceral allodynia and suggest that it is mediated by CCL2-driven mast cell accumulation in the bladder.

Sex Differences in Pain

Prevalence of lower urinary tract symptoms and level of quality of life in men and women with chronic pelvic pain.
Quaghebeur J, Wyndaele JJ.
Scand J Urol. 2014 Dec 2:1-8.
http://www.ncbi.nlm.nih.gov/pubmed/25438989

Objectives. The aim of this study was to evaluate the prevalence of lower urinary tract symptoms and quality of life in patients with chronic pelvic pain syndrome (CPPS). **Materials and methods**. The McGill Pain Questionnaire, Dutch Leiden/Leuven Version (MPQ-DLV), Pain Disability Index (PDI), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), Interstitial Cystitis Symptom Index (ICSI) and Pelvic Pain and Urinary/Frequency Symptom Scale (PUF) were used, based on their specific properties, to assess the symptoms and impact on the quality of life. Total scores and domains were compared for gender. **Results**. The studied group (N = 35; 18 male, 17 female) showed a good distribution in gender for age [Mann-Whitney U test (MW-U) p = 0.4] and body mass index (MW-U p = 0.2). The MPQ-DLV showed significantly higher scores for pain in women for Pain Rating Index - Affective (MW-U p = 0.030) and Total (MW-U p = 0.031), and Visual Analogue Scale for Pain - Most (MW-U p = 0.005). Women were less sexually active (PUF-SA) (chi-squared test p = 0.021) and had a significantly higher disability (PDI-T) (MW-U p = 0.005) and MPQ - Quality of Life (MW-U p = 0.003). The urinary symptoms showed similar results for gender (chi-squared test p > 0.05). **Conclusions**. A wide variety of symptoms and a negative impact on quality of life were shown. No differences in lower urinary tract symptoms were found between genders. Women were less sexually active than men. Chronic pelvic pain had a significantly higher negative impact on the level of quality of life in women than in men.