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## Vulvodynia

### Characteristics of the Vaginal Microbiome in Women With and Without Clinically Confirmed Vulvodynia

Lisa Bedford, Samantha E Parker, Elyse Davis, Elizabeth Salzman, Sharon L Hillier, Betsy Foxman, Bernard L Harlow

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<https://pubmed.ncbi.nlm.nih.gov/32135142/>

**Background:** Vulvodynia (idiopathic vulvar pain) affects up to 8% of women by age 40 years, has a poorly understood etiology, and has variable treatment efficacy. Several risk factors are associated with vulvodynia from a history of yeast infections to depression and allergies. Recent work suggests an altered immune-inflammatory mechanism plays a role in vulvodynia pathophysiology. Because the vaginal microbiome plays an important role in local immune-inflammatory responses, we evaluated the vaginal microbiome among women with vulvodynia compared with controls as 1 component of the immune system. **Objective:** The objective of the study was to characterize the vaginal microbiome in women with clinically confirmed vulvodynia and age-matched controls and assess its overall association with vulvodynia and how it may serve to modify other factors that are associated with vulvodynia as well. **Study design:** We conducted a case-control study of 234 Minneapolis/Saint Paul-area women with clinically confirmed vulvodynia and 234 age-matched controls clinically confirmed with no history of vulvar pain. All participants provided vulvovaginal swab samples for culture-based and non-culture (sequencing)-based microbiological assessments, background and medical history questionnaires on demographic characteristics, sexual and reproductive history, and history of psychosocial factors. Vaginal microbiome diversity was assessed using the Shannon alpha diversity Index. Data were analyzed using logistic regression. **Results:** Culture and molecular-based analyses of the vaginal microbiome showed few differences between cases and controls. However, among women with alpha diversity below the median (low), there was a strong association between increasing numbers of yeast infections and vulvodynia onset, relative to comparable time periods among controls (age-adjusted odds ratio, 8.1, 95% confidence interval, 2.9-22.7 in those with 5 or more yeast infections). Also among women with low-diversity microbiomes, we observed a strong association between moderate to severe childhood abuse, antecedent anxiety, depression, and high levels of rumination and vulvodynia with odds ratios from 1.83 to 2.81. These associations were not observed in women with high-diversity microbiomes.

**Conclusion:** Although there were no overall differences in microbiome profiles between cases and controls, vaginal microbiome diversity influenced associations between environmental and psychosocial risk factors and vulvodynia. However, it is unclear whether vaginal diversity modifies the association between the risk factors and vulvodynia or is altered as a consequence of the associations.

### **The International Classification of Diseases, 11th Revision: A Step-Back for Women With Vulvodynia?**

Gianluigi Radici, Mario Preti, Pedro Vieira-Baptista, Colleen K Stockdale, Jacob Bornstein

J Low Genit Tract Dis. 2020 Feb 14. doi: 10.1097/LGT.0000000000000513.

<https://pubmed.ncbi.nlm.nih.gov/32068619/>

**Objective:** The aim of the study was to compare the International Classification of Diseases, 11th revision, (ICD-11) with current terminology of vulvodynia, approved by a broad-based consensus of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS). **Methods:** The diagnostic criteria and descriptions of vulvodynia as well as the definition and classification of chronic pain in ICD-11 were reviewed and compared with the Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia, endorsed in 2015 by the ISSVD, ISSWSH, and IPPS. **Results:** Diagnostic criteria and descriptors of vulvodynia in the ICD-11 are outdated. Moreover, vulvodynia is not identified among chronic pain diagnoses, despite fulfilling the diagnostic criteria of chronic primary pain. Specifically, vulvodynia is a vulvar pain of at least 3-month duration, which is associated with significant emotional distress and functional disability, and is not better accounted for by another specific condition. **Conclusions:** The ICD-11 is not aligned with current vulvodynia diagnostic criteria and terminology, approved by the ISSVD, ISSWSH, and IPPS. Collaboration among the International Association for the Study of Pain Task Force on Classification of Chronic Pain, ICD team, ISSVD, ISSWSH, and IPPS is needed to harmonize terminologies, codes, and clinical approach regarding vulvar pain and vulvodynia classification.

### **Vulvodynia**

Sophie Bergeron, Barbara D Reed, Ursula Wesselmann, Nina Bohm-Starke

Nat Rev Dis Primers. 2020 Apr 30;6(1):36. doi: 10.1038/s41572-020-0164-2.

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Vulvodynia is a condition that occurs in 8-10% of women of all ages and is characterized by pain at the vulva that is present during sexual and/or non-sexual situations. Diagnosis is established through careful medical history and pelvic examination, including the cotton-swab test. The onset and maintenance of vulvodynia involves a complex interplay of peripheral and central pain mechanisms, pelvic floor muscle and autonomic dysfunction, anxiety, depression and childhood maltreatment as well as cognitive-affective, behavioural and interpersonal factors. Given the absence of empirically supported treatment guidelines, a stepwise approach of pelvic floor physical therapy and cognitive behavioural therapy as well as medical management is suggested, with surgery as the last option. Vulvodynia has a negative effect on the quality of life of women and their partners, and imposes a profound personal and societal economic burden. In addition, women with vulvodynia are more likely to report other chronic pain conditions, which further alters their quality of life. Future efforts should aim to increase girls', women's and healthcare professionals' education and awareness of vulvodynia, phenotype different subgroups of women based on biopsychosocial characteristics among more diverse samples, conduct longitudinal studies and improve clinical trial designs.

### **Vestibular Anatomic Localization of Pain Sensitivity in Women with Insertional Dyspareunia: A Different Approach to Address the Variability of Painful Intercourse**

Ahinoam Lev-Sagie, Osnat Wertman, oav Lavee, Michal Granot

J. Clin. Med. 2020, 9(7), 2023

<https://www.mdpi.com/2077-0383/9/7/2023/htm>

The pathophysiology underlying painful intercourse is challenging due to variability in manifestations of vulvar pain hypersensitivity. This study aimed to address whether the anatomic location of vestibular-provoked pain is associated with specific, possible causes for insertional dyspareunia. Women ( $n = 113$ ) were assessed for “anterior” and “posterior” provoked vestibular pain based on vestibular tenderness location evoked by a Q-tip test. Pain evoked during vaginal intercourse, pain evoked by deep muscle palpation, and the severity of pelvic floor muscles hypertonicity were assessed. The role of potential confounders (vestibular atrophy, umbilical pain hypersensitivity, hyper-tonus of pelvic floor muscles and presence of a constricting hymenal-ring) was analyzed to define whether distinctive subgroups exist. Q-tip stimulation provoked posterior vestibular tenderness in all participants ( $6.20 \pm 1.9$ ). However, 41 patients also demonstrated anterior vestibular pain hypersensitivity ( $5.24 \pm 1.5$ ). This group (circumferential vestibular tenderness), presented with either vestibular atrophy associated with hormonal contraception use ( $n = 21$ ), or augmented tactile umbilical-hypersensitivity ( $n = 20$ ). The posterior-only vestibular tenderness group included either women with a constricting hymenal-ring ( $n = 37$ ) or with pelvic floor hypertonicity ( $n = 35$ ). Interestingly, pain evoked during intercourse did not differ between groups. Linear regression analyses revealed augmented coital pain experience, umbilical-hypersensitivity and vestibular atrophy predicted enhanced pain hypersensitivity evoked at the anterior, but not at the posterior vestibule ( $R = 0.497$ ,  $p < 0.001$ ). Distinguishing tactile hypersensitivity in anterior and posterior vestibule and recognition of additional nociceptive markers can lead to clinical subgrouping.

### **Expression of Estrogen-Related Receptors in Localized Provoked Vulvodynia**

Anu Aalto, Riitta Huotari-Orava, Satu Luhtala, Johanna Mäenpää, Synnöve Staff

Biores Open Access. 2020 Feb 21;9(1):13-21. doi: 10.1089/biores.2019.0049. eCollection 2020.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7047250/>

Eight percent of women suffer from vulvodynia, a chronic pain condition with unknown etiology. Inflammation and dysregulation of estrogen signaling have been suggested to play a role in the pathogenesis of localized provoked vulvodynia (LPV). Therefore, the aim of the study was to analyze protein expression levels of estrogen-related receptors  $ERR\alpha$ ,  $ERR\beta$ ,  $ERR\gamma$ , estrogen receptor ( $ER\alpha$ ), and progesterone receptor ( $PR\alpha$ ) and CD3-positive T cells in the vulvar vestibulum obtained from women suffering from LPV in comparison to healthy, unaffected controls. Vulvar vestibulum tissue specimens were obtained from LPV patients ( $n = 12$ ) who had undergone modified posterior vestibulectomy and from 15 healthy controls. Protein expression of  $ERR\alpha$ ,  $ERR\beta$ ,  $ERR\gamma$ ,  $ER\alpha$ , and  $PR\alpha$  and CD3-positive T cells was analyzed by immunohistochemistry (IHC). Expression of  $ERR\beta$  was significantly more pronounced in samples from LPV compared to healthy controls ( $p = 0.006$ ). No significant difference in the expression patterns of  $ERR\alpha$ ,  $ERR\gamma$ ,  $ER\alpha$ ,  $PR\alpha$ , or CD3 cells was detected. To our knowledge, this is the first study reporting  $ERR$  expression in normal vestibulum and in vestibulectomy samples from LPV patients. The higher level of  $ERR\beta$  expression detected by IHC may reflect dysregulation of estrogen signaling in LPV.

## **Self-Focused Reasons for Having Sex: Associations Between Sexual Goals and Women's Pain and Sexual and Psychological Well-being for Couples Coping With Provoked Vestibulodynia**

Serena Corsini-Munt, Sophie Bergeron, Natalie O Rosen

J Sex Med. 2020 May;17(5):975-984. doi: 10.1016/j.jsxm.2020.01.017. Epub 2020 Mar 6.

<https://pubmed.ncbi.nlm.nih.gov/32147313/>

**Background:** For couples coping with provoked vestibulodynia (PVD), interpersonal sexual goals are associated with sexual and psychological functioning as well as women's pain during intercourse, however, self-focused sexual goals (eg, having sex for personal pleasure, having sex to avoid feeling bad about oneself) have not been studied in this clinical population. **Aim:** The purpose of this study was to examine the associations between self-focused approach and avoidance sexual goals and women's pain during intercourse and sexual satisfaction and depressive symptoms for both women and their partners. **Methods:** Women diagnosed with PVD (N = 69) and their partners completed measures of self-focused sexual goals, sexual satisfaction, and depressive symptoms. Women also reported on pain experienced during sexual intercourse. **Outcomes:** Outcomes included the Global Measure of Sexual Satisfaction, the Beck Depression Inventory-II, and a Numerical Rating Scale of pain during sexual intercourse. **Results:** When women reported higher self-focused approach sexual goals, they also reported lower pain intensity. Women's higher self-focused avoidance sexual goals were associated with their own higher depressive symptoms, whereas men's higher self-focused approach goals were associated with their own higher depressive symptoms. When controlling for frequency of sexual intercourse, there were no significant associations between women or partners' sexual goals and sexual satisfaction. **Clinical implications:** Within a clinical context where many interpersonal pressures for sex exist, interventions should target self-focused sexual goals alongside interpersonal sexual goals to improve pain and psychological adjustment. **Strengths & limitations:** This is the first study to examine self-focused sexual goals among women with PVD and their partners. This study is cross-sectional, and the direction of associations cannot be inferred. Couples were in mixed-sex relationships, and results may not generalize to same-sex couples. **Conclusion:** Findings suggest that self-focused goals are relevant to the psychological adjustment of women with PVD and their male partners and for women's pain. Corsini-Munt S, Bergeron S, Rosen NO. Self-Focused Reasons for Having Sex: Associations Between Sexual Goals and Women's Pain and Sexual and Psychological Well-being for Couples Coping With Provoked Vestibulodynia.

## **An Attachment Perspective on Partner Responses to Genito-pelvic Pain and Their Associations With Relationship and Sexual Outcomes**

Véronique Charbonneau-Lefebvre, Natalie O Rosen, Myriam Bosisio, Marie-Pier Vaillancourt-Morel, Sophie Bergeron

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<https://pubmed.ncbi.nlm.nih.gov/32432494/>

Although facilitative and negative partner responses are known to impact couples' adaptation to provoked vestibulodynia (PVD), a chronic genito-pelvic pain condition, it is still unknown what leads individuals to adopt or perceive such adaptative or detrimental behaviors. Attachment influences sexual and relationship adjustment, emotional reactivity and perceived support in romantic relationships, and as such could be associated with partner responses. This study aimed at examining the mediating role of facilitative and negative partner responses in the associations between attachment and relationship and sexual adjustment in 125 couples coping with PVD. Couples completed self-report questionnaires on attachment, partner responses, sexual satisfaction and distress, and relationship satisfaction. Results

indicated that partners' attachment avoidance was negatively associated with facilitative partner-reported responses, which in turn was associated with partners' sexual and relationship satisfaction. Attachment anxiety in women and partners was associated with greater women-perceived negative partner responses, which in turn was associated with women's and partners' greater sexual distress and lower sexual satisfaction, and women's lower relationship satisfaction. Partners' greater attachment anxiety was also associated with greater partner-reported facilitative responses, which was associated with partners' lower and women's greater relationship satisfaction. Assessing attachment orientations may help clinicians better understand couples' dyadic coping.

## Co-morbid Disorders

### **Normative values for Glazer Protocol in the evaluation of pelvic floor muscle bioelectrical activity**

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Medicine (Baltimore). 2020 Jan; 99(5): e19060. Published online 2020 Jan 31.

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<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7004594/>

The aim of the study was to evaluate pelvic floor muscle bioelectrical activity in healthy, young, and nulliparous women, and to present normative values for all phases and parameters measured with the Glazer Protocol.

In this study, 96 healthy, young, nulliparous women (age 22–27 years; 168.6 ± 5.1 cm; 57.1 ± 11.8 kg) were tested. The bioelectrical activity of the pelvic floor muscles was collected using an endovaginal electrode with the Glazer Protocol, which included the following series of muscles contractions and relaxations: pre-baseline rest, phasic contractions, tonic contractions, isometric contractions for muscle endurance evaluation, and post-baseline rest.

The following normative values of the bioelectrical signal for all phases of the Glazer Protocol were calculated: mean, minimal, and maximal values, 95% confidence interval, standard deviation, 95% standard deviation confidence interval, variance, coefficient of variation, and standard error of measurement. Average Mean Amplitude (μV) was as follows: pre-baseline rest (6.26 ± 3.33 μV), phasic contractions (49.76 ± 26.44 μV), tonic contractions (37.05 ± 25.99 μV), endurance contraction (16.10 ± 6.68 μV), and post-baseline rest (6.93 ± 3.99 μV).

This study was the first in which normative values for all phases of the Glazer Protocol were reported. This protocol is very often used in electromyography devices as a tool for pelvic floor muscle assessment. Due to the fact that the interpretation of the pelvic floor muscle evaluation is complex and difficult, the authors believe that the normative values proposed in this study allow for comprehensive interpretation of this test (both qualitatively and quantitatively) and provide a reference point for parameters measured in women with different pelvic floor dysfunctions.

### **How Does Myofascial Physical Therapy Attenuate Pain in Chronic Pelvic Pain Syndrome?**

Keren Grinberg, Irit Weissman-Fogel, Lior Lowenstein, Liora Abramov, and Michal Granot  
Pain Res Manag. 2019; 2019: 6091257. Published online 2019 Dec 12. doi: 10.1155/2019/6091257

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6930783/>

**Background:** Chronic pelvic pain syndrome (CPPS) is a multifactorial disorder comprising structural and functional muscular abnormalities, a dysfunctional pain system, and psychological distress. Myofascial physical Therapy (MPT) that is targeted at improving pelvic muscle functioning is considered a first line nonpharmacological treatment for CPPS, although the precise mechanisms that lead to symptoms alleviation have not yet been elucidated. **Purpose:** This longitudinal study aimed to examine the local and systemic effects of MPT intervention, including biopsychophysiological processes, among CPPS patients. **Methods:** The study included 50 CPPS women. Morphologic assessment of the levator ani and quantitative sensory testing of the pain system were applied alongside with evaluation of pain-related psychological factors using designated questionnaires. All measures were evaluated both before and after MPT in 39 patients. The long-term effects of MPT were evaluated by clinical pain reports obtained at 3 and 9 months following MPT that were compared with a nontreated group of 11 untreated CPPS women. **Results:** Along with an improvement in the clinical pain intensity ( $p = 0.001$ ) and sensitivity to experimental pain tests ( $p = 0.001$ ) following MPT, the results also indicate that MPT has anatomical, psychological, and social therapeutic effects ( $p = 0.04$ ;  $p = 0.001$ ;  $p = 0.01$ , respectively). Furthermore, clinical pain evaluation at 3 and 9 months after MPT revealed a significant improvement in women who received treatment ( $p = 0.001$ ). **Conclusions:** The findings of this pilot study suggest multisystemic (direct and indirect anatomical, neurophysiological, and psychological) effects of MPT on the multifactorial pain disorder of CPPS and therefore place MPT as a mechanism-based intervention.

#### **Commentary: The Vaginal and Urinary Microbiomes in Premenopausal Women With Interstitial Cystitis/Bladder Pain Syndrome as Compared to Unaffected Controls: A Pilot Cross-Sectional Study**

Magdalena Emilia Grzybowska

Front Cell Infect Microbiol. 2020; 10: 64. Published online 2020 Feb 25. doi: 10.3389/fcimb.2020.00064  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7052285/>

In this article, Meriwether et al. have assessed the vaginal and urinary microbiome to detect alterations associated with the presence of Interstitial cystitis/bladder pain syndrome (ICBPS). The study group included 23 women with ICBPS and 18 controls. No significant differences were found in the vaginal or urinary microbiome between the groups. ICBPS women presented lower scores in the applied questionnaires: Overactive Bladder Questionnaire, Pelvic Floor Distress Inventory-20, modified Body Image Scale and several Pelvic Organ Prolapse/Incontinence Sexual Questionnaire – IUGA Revised (PISQ-IR) domains in sexually active women. My main doubt concerns the PISQ-IR calculation system, which could influence the obtained results.

#### **Persistent genital arousal disorder: a special sense neuropathy**

Anne Louise Oaklander, Saurabh Sharma, Katie Kessler, and Bruce H. Price

Pain Rep. 2020 Jan-Feb; 5(1): e801. Published online 2020 Jan 7. doi: 10.1097/PR9.0000000000000801  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7004503/?report=classic>

**Introduction:** Persistent genital arousal (PGAD) is a syndrome of unprovoked sexual arousal/orgasm of uncertain cause primarily reported in female patients. Most patients are referred for mental-health treatment, but as research suggests associations with neurological symptoms and conditions, there is need to analyze cases comprehensively evaluated by neurologists. **Methods:** The IRB waived consent requirements for this retrospective university-hospital study. We extracted and analyzed neurological symptoms, test, and treatment results from all qualifying participants' records and recontacted some for details. **Results:** All 10 participants were female; their PGAD symptoms began between ages 11 to 70

years. Two patterns emerged: 80% reported daily out-of-context sexual arousal episodes ( $\leq 30$ /day) that usually included orgasm and 40% reported lesser, often longer-lasting, nonorgasmic arousals. Most also had symptoms consistent with sacral neuropathy—70% had urologic complaints and 60% had neuropathic perineal or buttock pain. In 90% of patients, diagnostic testing identified anatomically appropriate and plausibly causal neurological lesions. Sacral dorsal-root Tarlov cysts were most common (in 4), then sensory polyneuropathy (2). One had spina bifida occulta and another drug-withdrawal effect as apparently causal; lumbosacral disc herniation was suspected in another. Neurological treatments cured or significantly improved PGAD symptoms in 4/5 patients, including 2 cures.

**Conclusions:** Although limited by small size and referral bias to neurologists, this series strengthens associations with Tarlov cysts and sensory polyneuropathy and suggests new ones. We hypothesize that many cases of PGAD are caused by unprovoked firing of C-fibers in the regional special sensory neurons that subserve sexual arousal. Some PGAD symptoms may share pathophysiologic mechanisms with neuropathic pain and itch.

### Functioning During a Pandemic

Irwin Goldstein, MD, Editor-in-Chief

Sex Med Rev. 2020 Jun 15 doi: 10.1016/j.sxmr.2020.05.002

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7295483/>

The world has turned upside down, yet we continue. More deaths occurred in the United States than during the Vietnam War. As I write this editorial, more than 7.5 million people have been diagnosed with coronavirus worldwide, and more than 400,000 have died, with a rate of almost 150,000 new cases per day. Yet, we go to sleep each night assuming we are going to wake up tomorrow morning. How has this affected us as sexual medicine clinicians and researchers and educators?

### Application of Botulinum Neurotoxin in Female Sexual and Genitourinary Dysfunction: A Review of Current Practices

Brian Dick, Caleb Natale, Amit Reddy, Kole Prasad Akula, Ayad Yousif, Wayne J G Hellstrom

Sex Med Rev. 2020 Mar 29;S2050-0521(20)30007-X. doi: 10.1016/j.sxmr.2020.01.003.

<https://pubmed.ncbi.nlm.nih.gov/32238326/>

**Introduction:** The past 2 decades have witnessed an increased amount of research into botulinum neurotoxin (BoNT) as a treatment for various forms of sexual dysfunction and pain syndromes refractory to other medical therapy. BoNT is postulated to reduce pain sensation by inhibiting neuropeptide release in the presynaptic neuron. Dyspareunia, vaginismus, vestibulodynia, and persistent genital arousal disorder are female sexual dysfunctions with cryptic pathophysiology and limited treatment options. BoNT has emerged as a potential treatment for many of these afflictions in women. **Objectives:** To review the literature regarding BoNT as a treatment for female sexual and genitourinary dysfunction.

**Methods:** A PubMed search for English-language articles was performed using the following terms: "Botox," "botulinum toxin," "botulinum toxin A," "Onabotulinum A," "Abobotulinum A," "BoNT," and "BoNT-A." The main outcomes measured by each study were resolution of dysfunction. This entailed reduction of pain with intercourse for dyspareunia, reduction of pain for vestibulodynia, decreased arousal for persistent genital arousal disorder, and ability to tolerate penetration for vaginismus.

**Results:** A total of 12 human studies that evaluated BoNT as a treatment for female sexual disorders were included. Study types included prospective, retrospective, cohort, pilot, and open-label.

**Conclusion:** There is growing evidence suggesting that BoNT is a safe and efficacious treatment option for female patients suffering from various sexual and genitourinary disorders. However, more research is needed to develop a better understanding of the mechanisms through which BoNT treats these disorders. Dick B, Natale C, Reddy A, et al. Application of Botulinum Neurotoxin in Female Sexual and Genitourinary Dysfunction: A Review of Current Practices. *Sex Med* 2020;XX:XXX-XXX.

### **Can Botulinum Toxin A Play a Role in Treatment of Chronic Pelvic Pain Syndrome in Female Patients?—Clinical and Animal Evidence**

Chin-Li Chen and En Meng

*Toxins* (Basel). 2020 Feb; 12(2): 110. Published online 2020 Feb 10. doi: 10.3390/toxins12020110

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7076794/?report=classic>

Chronic pelvic pain (CPP) is defined as chronic pain and inflammation in the pelvic organs for more than six months. There are wide ranges of clinical presentations, including pelvic pain, painful intercourse, irritable bowel syndrome, and pain during urinating. Chronic pelvic pain syndrome (CPPS) is a subdivision of CPP, and the pain syndrome may be focused within a single organ or more than one pelvic organ. As there is uncertain pathogenesis, no standard treatment is currently available for CPPS. Botulinum toxin A (BoNT-A) is a potent neurotoxin that blocks acetylcholine release to paralyze muscles. Intravesical BoNT-A injection can reduce bladder pain in patients with interstitial cystitis/bladder pain syndrome. BoNT-A injected into the pelvic floor muscles of women has also been reported to improve chronic pain syndrome. Due to the reversible effect of BoNT-A, repeated injection appears to be necessary and effective in reducing symptoms. Adverse effects of BoNT-A may worsen the preexisting conditions, including constipation, stress urinary incontinence, and fecal incontinence. This review summarizes the evidence of BoNT-A treatment for CPPS in animal studies and clinical studies regarding the therapeutic effects of BoNT-A for CPPS in female patients.

### **Status, challenges, and future prospects of stem cell therapy in pelvic floor disorders**

Juan Cheng, Zhi-Wei Zhao, Ji-Rui Wen, Ling Wang, Li-Wei Huang, Yan-Lin Yang, Feng-Nian Zhao, Jing-Yue Xiao, Fei Fang, Jiang Wu, and Ya-Li Miao

*World J Clin Cases*. 2020 Apr 26; 8(8): 1400–1413. Published online 2020 Apr 26

doi: 10.12998/wjcc.v8.i8.1400

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7190946/>

Pelvic floor disorders (PFDs) represent a group of common and frequently-occurring diseases that seriously affect the life quality of women, generally including stress urinary incontinence and pelvic organ prolapse. Surgery has been used as a treatment for PFD, but almost 30% of patients require subsequent surgery due to a high incidence of postoperative complications and high recurrence rates. Therefore, investigations of new therapeutic strategies are urgently needed. Stem cells possess strong multi-differentiation, self-renewal, immunomodulation, and angiogenesis abilities and they are able to differentiate into various cell types of pelvic floor tissues and thus provide a potential therapeutic approach for PFD. Recently, various studies using different autologous stem cells have achieved promising results by improving the pelvic ligament and muscle regeneration and conferring the tissue elasticity and strength to the damaged tissue in PFD, as well as reduced inflammatory reactions, collagen deposition, and foreign body reaction. However, with relatively high rates of complications such as bladder stone formation and wound infections, further studies are necessary to investigate the role of stem cells as maintainers of tissue homeostasis and modulators in early interventions including



therapies using new stem cell sources, exosomes, and tissue-engineering combined with stem cell-based implants, among others. This review describes the types of stem cells and the possible interaction mechanisms in PFD treatment, with the hope of providing more promising stem cell treatment strategies for PFD in the future.

### **Vulvar pruritus-Causes, Diagnosis and Therapeutic Approach**

Linn Woelber, Katharina Prieske, Werner Mendling, Barbara Schmalfeldt, Hans-Jürgen Tietz, Anna Jaeger  
Dtsch Arztebl Int. 2020 Feb 21;116(8):126-133. doi: 10.3238/arztebl.2020.0126.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7081372/>

**Background:** In Germany, 17–23% of the population suffers from chronic itching of the skin; in 5–10% of cases, the female genitalia are affected, specifically, the vulva. Vulvar pruritus is thus a common symptom that often markedly impairs the affected women’s quality of life. **Methods:** This review is based on pertinent publications that were retrieved by a selective search in MEDLINE/PubMed for articles on the pathogenesis, diagnosis, and treatment of vulvar pruritus. The search terms were (in German and English) “vulvärer Juckreiz,” “pruritus vulvae,” and “genital itch,” alone and in combination with “Behandlung,” “Therapie,” or “treatment.” **Results:** The most common cause of vulvar pruritus is vulvovaginal candidiasis followed by chronic dermatoses, such as lichen sclerosus and vulvar eczema. Especially in refractory cases, an invasive or preinvasive lesion such as squamous epithelial dysplasia (VIN, vulvar intraepithelial neoplasia) should be borne in mind in the differential diagnosis. Rarer causes include infection, atrophy, and vulvodynia. The essential elements of treatment are topical/oral antimycotic drugs and high-potency glucocorticoids, along with consistently applied, basic moisturizing care and the avoidance of potential triggering factors. **Conclusion:** As vulvar pruritus has multiple causes, standardization of its diagnostic evaluation and treatment would be desirable, both to achieve optimal efficacy and to meet the diverse needs of women who suffer from this condition.

### **Application of Adult and Pluripotent Stem Cells in Interstitial Cystitis/Bladder Pain Syndrome Therapy: Methods and Perspectives**

Ahmed Abdal Dayem, Kyeongseok Kim, Soo Bin Lee, Aram Kim, and Ssang-Goo Cho

J Clin Med. 2020 Mar; 9(3): 766. Published online 2020 Mar 12. doi: 10.3390/jcm9030766

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7141265/>

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a multifactorial, chronic disease without definite etiology characterized by bladder-related pelvic pain. IC/BPS is associated with pain that negatively affects the quality of life. There are various therapeutic approaches against IC/BPS. However, no efficient therapeutic agent against IC/BPS has been discovered yet. Urothelium dysfunction is one of the key factors of IC/BPS-related pathogenicity. Stem cells, including adult stem cells (ASCs) and pluripotent stem cells (PSCs), such as embryonic stem cells (ESCs) and induced PSCs (iPSCs), possess the abilities of self-renewal, proliferation, and differentiation into various cell types, including urothelial and other bladder cells. Therefore, stem cells are considered robust candidates for bladder regeneration. This review provides a brief overview of the etiology, pathophysiology, diagnosis, and treatment of IC/BPS as well as a summary of ASCs and PSCs. The potential of ASCs and PSCs in bladder regeneration via differentiation into bladder cells or direct transplantation into the bladder and the possible applications in IC/BPS therapy are described in detail. A better understanding of current studies on stem cells and bladder regeneration will allow further improvement in the approaches of stem cell applications for highly efficient IC/BPS therapy.

### **New Insights about Chronic Pelvic Pain Syndrome (CPPS)**

Keren Grinberg, Yael Sela, and Rachel Nissanholtz-Gannot

Int J Environ Res Public Health. 2020 May; 17(9): 3005. Published online 2020 Apr 26. doi: 10.3390/ijerph17093005

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7246747/>

**Background:** Chronic pelvic pain syndrome (CPPS) is one of the common diseases in urology and gynecology. CPPS is a multifactorial disorder where pain may originate in any of the urogynecological, gastrointestinal, pelvic musculoskeletal, or nervous systems. The symptoms of CPPS appear to result from an interplay between psychological factors and dysfunction in the immune, neurological, and endocrine systems. The aim of this article was to present new insight about CPPS in order to raise awareness of nursing and medical staff in the identification and diagnosis of the syndrome and to promote an appropriate treatment for each woman who suffers from CPPS. **Methods:** A literature review about the factors associated with CPPS and therapeutic interventions for CPPS was conducted. **Results:** CPPS represents a chronic pain syndrome that combines anatomic malfunction of the pelvic floor muscles with malfunction of pain perception linked with psychological and cognitive factors. **Conclusions:** The therapeutic interventions in CPPS cases should, consequently, follow a multidisciplinary approach.

### **Abstracts from the International Pelvic Pain Society (IPPS) Annual Scientific Meeting on Pelvic Pain 2019**

Georgine Lamvu, MD, MPH

Pain Rep. 2020 Mar-Apr; 5(2): e815. Published online 2020 Mar 19  
doi: 10.1097/PR9.0000000000000815

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7209814/>

### **Clitoral leiomyoma in a premenopausal woman: a case report**

Gianmarco Taraschi, Diego Aguiar, Jean Christophe Tille, Patrick Petignat, and Jasmine Abdulcadir

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**Background:** Extrauterine leiomyomata is an uncommon lesion that can lead to several problems of differential diagnosis, especially when localized in the external genitalia. There are few reports in the English literature and a novel association with Alport's syndrome has been investigated since the 1980s. **Case presentation:** Here, we describe the case of a premenopausal woman who presented with an indolent swelling of the right interlabial fossa that resulted in a Bartholin cyst. In addition to this cyst, a benign leiomyoma of the right side of the clitoris was also found and removed. Our patient refused any further examination, although she was informed that genetic counselling could be organized to rule out an association with Alport's syndrome. **Conclusions:** Extrauterine leiomyomata localized in the external genitalia is an uncommon lesion arising from smooth muscle cells around vascular epithelium or erectile tissue. Since an association between extrauterine leiomyomata and Alport's syndrome has been described, genetic testing can be proposed to these patients. Upper intestinal tract symptoms such as dysphagia should prompt a gastroenterological evaluation as an association with an esophageal leiomyomatosis has been described.

## Challenges in the Practice of Sexual Medicine in the Time of COVID-19 in the United States

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The 2019 Coronavirus disease (COVID-19) has in a period of just months completely upended travel, commerce, and daily life throughout the world. Medical practitioners have been forced to care for a surge of ill patients, in many cases, without access to testing and appropriate protective equipment. The impact of COVID-19 on research has been no less profound, with restrictions in terms of access and funding. The disease has been politicized from many angles; the economic consequences of this crisis will be long-lasting and unpredictable. For sexual medicine providers, the effects of COVID-19 are also numerous and multifactorial. In this article, we highlight some key aspects of the effects of COVID-19 on sexual medicine and how we can respond.

### Dermatological Conditions

#### Safety and Efficacy of Stromal Vascular Fraction Enriched Fat Grafting Therapy for Vulvar Lichen Sclerosus

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**Background:** Lichen sclerosus is an inflammatory dermatosis of unknown etiology which currently has no cure. Most treatment guidelines recommend the use of ultrapotent topical corticosteroids. However, the relapse rate is usually high. Through a retrospective study we evaluated the efficacy and safety of stromal vascular fraction of adipose tissue as therapy for lichen sclerosus. **Material and methods:** For this retrospective review, we obtained data on patients with vulvar lichen sclerosus treated with autologous fat grafting enriched with adipose derived stromal vascular fraction cells. Data collected through a modified vulvo-vaginal symptoms questionnaire were analyzed before treatment, six months and 24 months after treatment. The 19 items questionnaire was subdivided in four categories: symptoms, signs, social functioning and sexual functioning. Global scores and partial scores for each category were analyzed using paired t-test. For all statistical analyses, a value of  $p \leq 0.05$  was considered statistically significant. All data are presented as mean  $\pm$  SD. **Results:** Thirty nine patients were included in the study. Thirty seven patients (94.87%) experienced a significant decrease in global score at six months and 24 months after treatment ( $p < 0.05$ ). Decrease in scores were also statistically significant between pretreatment and 24 months after treatment for each of the four questionnaire categories - symptoms, signs, social functioning and sexual functioning ( $p < 0.05$ ). **Conclusions:** This retrospective study showed that the use of autologous fat grafting enriched with adipose derived stromal vascular fraction is safe and leads to significant and long lasting improvement in patients with vulvar lichen sclerosus.

## Comparison of topical clobetasol propionate 0.05% and topical tacrolimus 0.1% in the treatment of cutaneous lichen planus

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**Introduction:** The effectiveness of topical tacrolimus in the treatment of oral and genital lichen planus has been verified in many randomized studies; however, there are only few case reports in treatment of cutaneous lichen planus (CLP). **Aim:** We sought to compare the safety and efficacy of topical clobetasol propionate and tacrolimus ointment in the treatment of CLP. **Material and methods:** Retrospective analysis of patient files was performed. We enrolled patients who were diagnosed with CLP and treated with topical tacrolimus 0.1% or topical clobetasol propionate 0.05%. Visual Analogue Scale (VAS) scores of pigmentation and pruritus, clinical response, laboratory data and adverse effects were obtained from medical records. **Results:** A total of 27 patients were included in the clobetasol group and 23 patients in the tacrolimus group. Both groups showed an improvement in VAS scores regarding pruritus and pigmentation but a statistically significant difference was observed in the clobetasol group ( $p < 0.05$ ). At week 12, a complete response was observed in 63% ( $n = 17$ ) of the clobetasol and 26% ( $n = 6$ ) of the tacrolimus group. **Conclusions:** In our study, both treatments were found effective in the treatment of CLP but clobetasol propionate was more effective. However tacrolimus may be preferred before topical corticosteroids for lesions on the face, neck, and intertriginous regions of the body, which are sensitive to the cutaneous adverse effects of topical corticosteroids. Our study may be one of the first studies to compare the effects of topical clobetasol and tacrolimus ointment in the management of CLP.

## Etiology, Clinical Features, and Diagnosis of Vulvar Lichen Sclerosus: A Scoping Review

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**Objective:** Vulvar lichen sclerosus (VLS) is a chronic inflammatory disorder, which affects women of all ages. With numerous controversies as regards to the nomenclature, diagnosis and its association with neoplastic conditions, we decided to conduct a scoping review on this subject. **Data Source:** A review protocol was developed, and the Knowledge Resource Services website was used to do a search of articles pertaining to VLS with keywords “Vulvar,” “Vulval,” “diagnosis,” “lichen sclerosus et atrophicus,” “kraurosis,” “vulvar dystrophy,” and “Lichen Sclerosus”. **Study Selection:** The search was limited to published data from the last ten years, i.e., from July 2009 onwards and in the English language. A total of 338 articles pertaining to VLS were obtained. Older data were accessed if particular information was sought for. **Results & Conclusion:** The presentation is bimodal, i.e., one in prepubertal girls (average age: 7.6 years) and the other in peri- and postmenopausal women (average age: 52.6 years). However, many cases also present during reproductive years. Studies suggest a multifactorial origin as far as etiology is concerned, including a genetic, autoimmune, hormonal, and local infectious background. It affects the genital labial, perineal, and perianal areas and manifests as a patchy, thin, glistening, ivory-white area. Diagnosis is mainly based on clinical features. Biopsy is seldom required. It has been well established as a precursor lesion of dVIN and vulvar carcinoma.

## **Clonal Relationship Between Lichen Sclerosus, Differentiated Vulvar Intra-epithelial Neoplasia and Non HPV-related Vulvar Squamous Cell Carcinoma**

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**Background/Aim:** Differentiated vulvar intraepithelial neoplasia (dVIN) and lichen sclerosus (LS) can give rise to vulvar squamous cell carcinoma (VSCC), but genetic evidence is currently still limited. We aimed to determine genetic abnormalities in VSCC and backtrack these abnormalities in the dVIN and LS lesions. **Materials and Methods:** DNA from VSCC and patient-matched dVIN and LS samples of twelve patients was collected. High-resolution genome-wide copy number analysis was performed and subsequently, we sequenced TP53. **Results:** Copy number alterations were identified in all VSCC samples. One dVIN lesion presented with three copy number alterations that were preserved in the paired VSCC sample. Targeted sequencing of TP53 identified mutations in five VSCCs. All five mutations were traced back in the dVIN (n=5) or the LS (n=1) with frequencies ranging from 3-19%. **Conclusion:** Our data provide genetic evidence for a clonal relationship between VSCC and dVIN or LS.