Vulvodynia

Itraconazole Improves Vulvodynia in Fungus Culture-Negative Patients Post Fluconazole Failure
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Sex Med. 2021 Jul 8;9(4):100383. doi: 10.1016/j.esxm.2021.100383.
https://pubmed.ncbi.nlm.nih.gov/34246854/

Introduction: Vulvodynia is a difficult condition to treat due to both the uncertain etiology of the disorder and poorly available therapies. This difficulty leads to a disproportionately high prevalence and cost of treatment for this condition. Candida vulvovaginitis is a frequent co-present diagnosis in vulvodynia patients. Whether through treatment of co-present, candida vulvovaginitis or by systemic interaction, itraconazole has been proposed as a treatment for vulvodynia. Aim: To describe objective change in vulvodynia pain in a cohort of patients treated with itraconazole. Methods: This study was a retrospective cohort study comprised of women diagnosed with vulvodynia who were treated with itraconazole between January 1, 2011 and October 17, 2017. Patients had failed fluconazole treatment and had negative fungus cultures for >2 months before itraconazole treatment. All other vulvovaginal disorders were excluded. Main outcome measure: The main outcome measure was the change in pain before and after treatment as measured by cotton swab testing. Results: 106 patients met inclusion criteria. Average pain reduction for the entire cohort was 60.7%. Patients who continued itraconazole for 5 to 8 weeks demonstrated a 69.6% reduction in cotton swab test pain. Pain reduction as a percentage of total patients showed complete resolution of pain in 37.7% of patients and >50% reduction in 66.0% of patients. Two-sample paired T-tests for means analysis of pain scores disproved the null hypothesis (P < .01, α = 0.01) and showed a 50% reduction in pain to be significant (P = 0.043, α = 0.05). Two-tailed Wilcoxon signed rank test also demonstrated rejection of the null hypothesis (α = 0.05). Conclusions: Itraconazole therapy is associated with a significant reduction in vulvovaginal pain in patients with negative fungus cultures and no other identifiable disease in this pilot study. A randomized placebo-controlled trial is warranted.
Vulvodynia is one of the most common causes of pain during sexual intercourse in premenopausal women. The burden of vulvodynia in a woman's life can be devastating due to its consequences in the couple's sexuality and intimacy, in activities of daily living, and psychological well-being. In recent decades, there has been considerable progress in the understanding of vulvar pain. The most significant change has been the differentiation of vulvar pain secondary to pathology or disease from vulvodynia. However, although it is currently proposed that vulvodynia should be considered as a primary chronic pain condition and, therefore, without an obvious identifiable cause, it is still believed that different inflammatory, genetic, hormonal, muscular factors, etc. may be involved in its development. Advances in pain neuroscience and the central sensitization paradigm have led to a new approach to vulvodynia from a neurobiological perspective. It is proposed that vulvodynia should be understood as complex pain without relevant nociception. Different clinical identifiers of vulvodynia are presented from a neurobiological and psychosocial perspective. In this case, strategies to modulate altered central pain processing is necessary, changing the patient's erroneous cognitions about their pain, and also reducing fear avoidance-behaviors and the disability of the patient.

Potential for Selection Bias in Studies of the Association of Hormonal Contraception and Chronic Vulvar Pain
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https://pubmed.ncbi.nlm.nih.gov/34190629/

**Background:** Hormonal contraceptive use is common among reproductive-aged women, but research evaluating its etiological relationship to vulvodynia remains mixed. We sought to evaluate this association and examine the potential for bias due to care-seeking behavior. **Materials and Methods:** We conducted a case-control study of women recruited from a large health care network database from 2008 to 2011. Of 26,455 eligible respondents, 1168 met the case definition for chronic vulvar pain (CVP). We matched each case to three controls by age and used conditional logistic regression to calculate odds ratios (ORs) for prior hormonal contraception (HC) use and CVP, stratifying cases by whether or not they sought care for their vulvar pain. We also simulated the influence of potential biases due to care seeking, using parameters based on this dataset. **Results:** HC users had higher odds of CVP (adjusted OR = 2.6, 95% confidence interval [CI]: 2.2-3.2). Effect estimates were stronger when cases were restricted to care seekers (adjusted OR = 2.9, 95% CI: 2.2-3.7). Effect estimates decreased slightly as time increased between HC initiation and pain onset. Our simulations suggested that effect estimates may be spuriously strengthened when cases are restricted to care-seeking women, but controls are recruited from the general population. **Conclusions:** Our results suggest an association between antecedent HC use and CVP that is potentially spuriously strengthened in case-control studies when cases are restricted to care seekers but controls are not.
Efficacy of ganglion impar block on vulvodynia: Case series and results of mid- and long-term follow-up
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Medicine (Baltimore). 2021 Jul 30;100(30):e26799. doi: 10.1097/MD.00000000000026799.
https://pubmed.ncbi.nlm.nih.gov/34397737/

Rationale: Vulvodynia is a common chronic gynecological disease that affects approximately 16% of women, although it is rarely diagnosed. However, no known effective treatment exists. The etiology of vulvodynia is unknown and may be heterogeneous and multifactorial, so it is difficult—if not impossible—to improve this condition using 1 treatment method. Reports have shown that vulvodynia has an element of neuropathic pain. Although the role of the sympathetic nervous system in neuropathic pain is controversial, sympathetic nerve blocks have long been used to treat patients with chronic pain giving good results. A ganglion impar block (GIB), a sympathetic nerve block technique, may effectively manage pain and discomfort in patients with vulvodynia. Patient concerns: Four patients suffering from chronic vulvar pain for 6 months-10 years were referred by gynecologists. The gynecologists could not identify the cause of the chronic vulvar pain, and symptoms were not improving by conservative therapy with medication. Patients complained of various chronic vulvar pain or discomfort. The initial visual analog scale (VAS) scores were 8 or 9 out of 10, and Leeds assessment of neuropathic symptoms and signs pain scale score was more than 12 out of 24. The review of gynecological medical records confirmed whether they showed allodynia during the cotton swab test and hyperalgesia to pin-prick test. Diagnoses: All patients were diagnosed with vulvodynia. Interventions: All patients were treated with a GIB, once in 2 patients, 3 times in 1 patient, and 4 times (1 alcoholic neurolysis) in the other patient, under fluoroscopic guidance. Outcomes: After the procedures, the VAS score and the Leeds assessment of neuropathic symptoms and signs (LANSS) pain scale score were decreased to less than 2 and 5, respectively, in all patients. Follow-up observations for 6 months-2 years revealed that 2 patients' symptoms entirely or nearly entirely improved and did not require further treatment. The pain of the remaining patients were well controlled with medications only. Lessons: GIB is a good treatment option for patients suffering from chronic pain and discomfort caused by vulvodynia.

Mechanically Supporting Uterosacral Ligaments for the Relief of Provoked Vulvodynia: A Randomized Pilot Trial
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J Pain Res. 2021 May 19;14:1281-1288. doi: 10.2147/JPR.S296613. eCollection 2021.
https://pubmed.ncbi.nlm.nih.gov/34040432/

Purpose: Provoked vulvodynia (PV) is the most common cause of vulvar pain and dyspareunia. Although its etiology is unknown, it has been associated with musculoskeletal dysfunction. The inability of the lax uterosacral ligaments (USLs) to support the adjoining T11/L2 and S2-4 nerve plexuses is considered to cause PV. This study aimed to determine whether providing mechanical support to the USLs would improve PV. Patients and methods: PV patients were randomly divided into two groups. The participants in each group underwent sham manipulation (inserting a wide swab in the vagina without applying pressure) and trial manipulation (supporting the posterior fornix with a wide swab sufficiently broad to mechanically support the USLs). This was a cross-over trial, and the participants alternated between the sham and trial manipulation. Using a 0-10 visual analog pain scale (VAS), PV-associated
pain levels experienced by participants were recorded during each manipulation, and the results were compared with baseline levels. **Results:** The pain level significantly reduced with USL support compared with the baseline value and the sham manipulation pain level (P = 0.003). Pain during sham manipulation was not significantly different from that recorded at baseline. The average reduction in pain with USL support was 18.4% ± 2.2%. The manipulation order did not affect changes in the pain level during trial manipulation (P = 0.512). **Conclusion:** Applying mechanical support to the posterior fornix temporarily alleviates provoked vulvar pain in some women.

**Comparing Vestibule Examination Techniques: Light Touch, Serial Forces, and the Lidocaine Test**

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J Low Genit Tract Dis. 2021 Jul 1;25(3):236-242. doi: 10.1097/LGT.0000000000000605.
https://pubmed.ncbi.nlm.nih.gov/34016868/

**Objective:** The purpose of this study was to compare techniques and pain scales that assess tenderness in the vulvar vestibule in provoked vestibulodynia, using the cotton swab test and a vulvalgesiometer, and assess topical lidocaine solution with each. **Materials and methods:** This randomized study at a specialty vulvar clinic evaluated tender vestibules of reproductive-aged women with vestibulodynia using light rolling cotton swab touch at 6 sites and evaluated the vulvalgesiometer at 2 sites, randomizing the order of the initial tool. Participants reported pain using the Numerical Rating Scale 0-10 and the Verbal Pain Scale 0-3. With the vulvalgesiometer, the pain tolerance threshold was measured using forces of 10, 25, 50, 100, 200, and 300 g. After both initial tests, lidocaine 4% topical solution was applied for 3 minutes, and the test and vulvalgesiometer were repeated in the order initially performed, constituting the lidocaine test. Data analysis used t tests, Fisher exact tests, Wilcoxon signed rank tests, and Spearman rank correlation. **Results:** Sixteen patients completed the study, 8 starting with each instrument. Light swab touch evoked significant pain, and lidocaine reduced pain to zero or mild levels. The pain threshold was 25 g, and only 38% could tolerate testing past 100 g without lidocaine. The Verbal Pain Scale correlated well with the Numerical Rating Scale. **Conclusions:** Light rolling cotton swab touch using the 4-item verbal scale can map vestibulodynia tenderness that can be extinguished by lidocaine, consistent with distinguishing a mucosal condition. Forces by vulvalgesiometer of greater than 100-200 g may evoke pain other than mucosal allodynia.

**Dysregulation in sphingolipid signaling pathways is associated with symptoms and functional connectivity of pain processing brain regions in provoked vestibulodynia**

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J Pain. 2021 May 21;S1526-5900(21)00231-5. doi: 10.1016/j.jpain.2021.04.017.
https://pubmed.ncbi.nlm.nih.gov/34029688/

Provoked vestibulodynia (PVD) is a chronic pain disorder characterized by local hypersensitivity and severe pain with pressure localized to the vulvar vestibule. Despite decades of study, the lack of identified biomarkers has slowed the development of effective therapies. The primary aim of this study was to use metabolomics to identify novel biochemical mechanisms in vagina and blood underlying brain biomarkers and symptoms in PVD, thereby closing this knowledge gap. Using a cross-sectional case-control observational study design, untargeted and unbiased metabolomic profiling of vaginal fluid and plasma was performed in women with PVD compared to healthy controls. In women with PVD, we also obtained assessments of vulvar pain, vestibular and vaginal muscle tenderness, and 24-hour
symptom intensity alongside resting-state brain functional connectivity of brain regions involved in pain processing and modulation. Compared to healthy controls, women with PVD demonstrated differences primarily in vaginal (but not plasma) concentrations of metabolites of the sphingolipid signaling pathways, suggesting localized effects in vagina and vulvar vestibule rather than systemic effects. Our findings reveal that dysregulation of sphingolipid metabolism in PVD is associated with increased vulvar pain and muscle tenderness, sexual dysfunction, and decreased functional connectivity strength in pain processing/modulatory brain regions. This data collectively suggests that alterations in sphingolipid signaling pathways are likely an important molecular biomarker in PVD that could lead to new targets for therapeutic intervention.

Localized Provoked Vulvodynia-An Ignored Vulvar Pain Syndrome
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Front Cell Infect Microbiol. 2021 Jun 17;11:678961.doi: 10.3389 fcimb.2021.678961. eCollection 2021.
https://pubmed.ncbi.nlm.nih.gov/34222047/

Localized provoked vulvodynia (LPV) causes dyspareunia among reproductive aged women. We review the pathogenesis of LPV and suggest that LPV is an inflammatory pain syndrome of the vestibular mucosa triggered by microbial antigens in a susceptible host. Tissue inflammation and hyperinnervation are characteristic findings which explain symptoms and clinical signs. Education of health care providers of LPV is important since this condition is common, often unrecognized, and patients often become frustrated users of health care. Research is needed on the antigen triggers of the syndrome. Randomized clinical trials are needed to evaluate treatment modalities.

Co-morbid Disorders

Botulinum toxin A (Botox) injection into muscles of pelvic floor as a treatment for persistent pelvic pain secondary to pelvic floor muscular spasm: A pilot study
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Aust N Z J Obstet Gynaecol. 2021 Jun 15. doi: 10.1111/a jo.13396.
https://pubmed.ncbi.nlm.nih.gov/34128537/

Background: Persistent pelvic pain (PPP) remains an important cause of morbidity. Pelvic floor muscle spasm is an important contributor to PPP. Aims: The study's primary aim was to assess if botulinum toxin (BoNT) injection to pelvic floor muscles altered pain scores or quality of life (QoL) at six, 12 and 26 weeks. Secondary aims included investigating the impact of BoNT on opiate usage, examining the role of pain catastrophising, and assessing for complications. Materials and methods: A single-centre prospective cohort study enrolled 21 patients with PPP who had failed physiotherapy techniques. Each participant underwent BoNT injection to muscles of the pelvic floor and pudendal nerve block. Questionnaires and digital vaginal examinations were conducted at baseline, six, 12 and 26 weeks. Pain score quantification used visual analogue scales (VAS) and numerical rating scales (NRS). Other outcome assessments included The World Health Organization Quality of Life instrument (WHOQoL-BREF), Pain Catastrophising Scale (PCS), and modified Australian Pelvic Floor Questionnaire (APFQ). ACTRN12620000067976. Results: Following BoNT injection, median VAS scores decreased for all domains at six and 12 weeks, with VAS for dyspareunia significant at six weeks (P = 0.026). Scores returned to baseline by 26 weeks. Opiate usage was significantly less following BoNT injection, with a
percentage reduction of 23.8% (95% CI -48.3 to 0.7, P = 0.06). Sexual function improved significantly (P < 0.01), and at six months, four previously apareunic participants reported successful penetrative vaginal intercourse. Health-related QoL and PCS demonstrated sustained improvement (P = 0.02-0.05). NRS for muscle tenderness decreased for all assessed muscle groups (P < 0.001). **Conclusions:** BoNT requires further assessment as a treatment modality for select women with PPP.

**Pelvic Floor Physical Therapy for Pelvic Floor Hypertonicity: A Systematic Review of Treatment Efficacy**
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Sex Med Rev. 2021 Jun 11;S2050-0521(21)00012-3. doi: 10.1016/j.sxmr.2021.03.002.
https://pubmed.ncbi.nlm.nih.gov/34127429/

**Introduction:** Hypertonicity of the pelvic floor (PFH) is a disabling condition with urological, gynecological and gastrointestinal symptoms, sexual problems and chronic pelvic pain, impacting quality of life. Pelvic floor physical therapy (PFPT) is a first-line intervention, yet no systematic review on the efficacy of PFPT for the treatment of PFH has been conducted. **Objectives:** To systematically appraise the current literature on efficacy of PFPT modalities related to PFH. **Methods:** PubMed, Embase, Emcare, Web of Science, and Cochrane databases were searched from inception until February 2020. A manual search from reference lists of included articles was performed. Ongoing trials were reviewed using clinicaltrial.gov. Randomized controlled trials (RCTs), prospective - and retrospective cohorts and case-study analyses were included. Outcome measures were pelvic floor muscle tone and function, pain reports, sexual function, pelvic floor symptom scores, quality of life and patients' perceived effect. **Results:** The literature search resulted in 10 eligible studies including 4 RCTs, 5 prospective studies, and 1 case study published between 2000 and 2019. Most studies had a high risk of bias associated with the lack of a comparison group, insufficient sample sizes and non-standardized interventions. Six studies were of low and 4 of medium quality. All studies were narratively reviewed. Three of 4 RCTs found positive effects of PFPT compared to controls on five out of 6 outcome measures. The prospective studies found significant improvements in all outcome measures that were assessed. PFPT seems to be efficacious in patients with chronic prostatitis, chronic pelvic pain syndrome, vulvodynia, and dyspareunia. Smallest effects were seen in patients with interstitial cystitis and painful bladder syndrome. **Conclusion:** The findings of this systematic review suggest that PFPT can be beneficial in patients with PFH. Further high-quality RCTs should be performed to confirm the effectiveness of PFPT in the treatment of PFH.

**Efficacy and Safety of Drug Combinations for Chronic Pelvic Pain: Protocol for a Systematic Review**
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JMIR Res Protoc. 2021 May 17;10(5):e21909. doi: 10.2196/21909.
https://pubmed.ncbi.nlm.nih.gov/33999006/

**Background:** Chronic pelvic pain with various etiologies and mechanisms affects men and women and is a major challenge. Monotherapy is often unsuccessful for chronic pelvic pain, and combinations of different classes of medications are frequently prescribed, with the expectation of improved outcomes. Although a number of combination trials for chronic pelvic pain have been reported, we are not aware of any systematic reviews of the available evidence on combination drug therapy for chronic pelvic pain.
Objective: We have developed a protocol for a systematic review to evaluate available evidence of the efficacy and safety of drug combinations for chronic pelvic pain. Methods: This systematic review will involve a detailed search of randomized controlled trials investigating drug combinations to treat chronic pelvic pain in adults. The databases searched will include the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE from their inception until the date the searches are run to identify relevant studies. The primary outcome will be pain relief measured using validated scoring tools. Secondary outcomes, where reported, will include the following: adverse events, serious adverse events, sexual function, quality of life, and depression and anxiety. Methodological quality of each included study will be assessed using the Cochrane Risk of Bias Tool. Results: The systematic review defined by this protocol is expected to synthesize available good quality evidence on combination drug therapy in chronic pelvic pain, which may help guide future research and treatment choices for patients and their health care providers. Conclusions: This review will provide a clearer understanding of the efficacy and safety of combination pharmacological therapy for chronic pelvic pain.

Management of Patients when Superficial Venous Disease Arises from Pelvic Escape Points
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Semin Intervent Radiol. 2021 Jun;38(2):226-232. doi: 10.1055/s-0041-1729744. Epub 2021 Jun 3. https://pubmed.ncbi.nlm.nih.gov/34108810/

Chronic pelvic pain (CPP) is a common condition in women that carries with it significant morbidity. It is commonly seen in patients presenting to obstetrics and gynecology outpatient clinic visits. CPP is a presenting symptom of various pathologies including pelvic varicocele, pelvic adhesions, spastic colon syndrome, uterine fibroids, endometriosis, and psychosomatic disorders. Pelvic congestion syndrome has more recently been termed "pelvic venous insufficiency (PVI)" due to the underlying retrograde flow through incompetent ovarian and pelvic veins that are thought to cause the symptoms of CPP. Pelvic varices can commonly present alongside vulvar, perineal, and lower extremity varices. There are some predictable "escape pathways" for these varices that may present for interventional treatment. This article introduces the reader to current terminology, clinical presentation, diagnosis, and treatment of patients with pelvic varices due to PVI.

Non-venous Pelvic Pain and Roles for Pelvic Floor PT or Pudendal Nerve Blocks
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Tech Vasc Interv Radiol. 2021 Mar;24(1):100735. doi: 10.1016/j.tvir.2021.100735. Epub 2021 Apr 21. https://pubmed.ncbi.nlm.nih.gov/34147192/

Non-venous pelvic pain is a dilemma that can frustrate even the most patient of providers. Managing these conditions can be even more bewildering as they require a multidisciplinary approach in most cases. Diet and lifestyle modifications in addition to physical therapy, biofeedback, medications, surgery and integrative medicine modalities can be used alone or in combination to relieve symptoms and should be individualized after proper evaluation and diagnosis. Because most of these conditions are located in the area of pudendal nerve distribution, pudendal nerve blocks have been very successful in helping to control the pain symptoms and should be used judiciously. Here we discuss the common conditions and how physical therapy and pudendal nerve blocks play a significant role in treatment.
Ultrasound-guided injections in pelvic entrapment neuropathies
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J Ultrason. 2021 Jun 7;21(85):e139-e146. doi: 10.15557/JoU.2021.0023. Epub 2021 Jun 18.
https://pubmed.ncbi.nlm.nih.gov/34258039/

Pelvic entrapment neuropathies represent a group of chronic pain syndromes that significantly impede the quality of life. Peripheral nerve entrapment occurs at specific anatomic locations. There are several causes of pelvic entrapment neuropathies, such as intrinsic nerve abnormality or inflammation with scarring of surrounding tissues, and surgical interventions in the abdomen, pelvis and the lower limbs. Entrapment neuropathies in the pelvic region are not widely recognized, and still tend to be underdiagnosed due to numerous differential diagnoses with overlapping symptoms. However, it is important that entrapment neuropathies are correctly diagnosed, as they can be successfully treated. The lateral femoral cutaneous nerve, ischiadic nerve, genitofemoral nerve, pudendal nerve, ilioinguinal nerve and obturator nerve are the nerves most frequently causing entrapment neuropathies in the pelvic region. Understanding the anatomy as well as nerve motor and sensory functions is essential in recognizing and locating nerve entrapment. The cornerstone of the diagnostic work-up is careful physical examination. Different imaging modalities play an important role in the diagnostic process. Ultrasound is a key modality in the diagnostic work-up of pelvic entrapment neuropathies, and its use has become increasingly widespread in therapeutic procedures. In the article, the authors describe the background of pelvic entrapment neuropathies with special focus on ultrasound-guided injections.

Persistent Genital Arousal Disorder

The Use of Pramipexole to Treat Persistent Genital Arousal Disorder: A Case Report
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Sex Med. 2021 Jun 11;9(4):100372. doi: 10.1016/j.esxm.2021.100372.
https://pubmed.ncbi.nlm.nih.gov/34126431/

Introduction: Persistent Genital Arousal Disorder (PGAD) is defined as "spontaneous, intrusive, and unwanted genital arousal (tingling, throbbing, pulsating) in the absence of sexual interest and desire" and traditionally causes marked distress, embarrassment and shame. PGAD may be caused by starting, discontinuing, or making adjustments in certain antidepressants or other medications.

Aim: To report the case of a 36-year-old woman with PGAD, likely due to changes in her psychiatric medications, who was treated with pramipexole and experienced improvement in her PGAD symptoms.

Methods: Patient self-report and literature review. Written informed consent was obtained from the patient. Main outcome measure: Improvement in PGAD symptoms. Results: Patient reported improvement in her symptoms by "90%" on a low dose of pramipexole, although higher doses exacerbated her symptoms. Conclusions: It is likely that an effective treatment window exists for the treatment of PGAD with drugs that possess the ability to exert their control of dopaminergic transmission. This includes direct acting receptor agonists like pramipexole, which produce feedback inhibition. Limitations to their efficacy then involve co-treatments that counteract their ability to exert a dampening effect on hyperstimulated dopamine transmission. It is recommended that clinicians be aware of drugs taken by patients to treat psychiatric disorders that could induce PGAD symptoms, drugs recently discontinued where a rebound effect could lead to PGAD symptoms, and drug mechanisms that could counteract the effect of treatments for PGAD.
Persistent Genital Arousal Disorder (PGAD): A Clinical Review and Case Series in Support of Multidisciplinary Management
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Sex Med Rev. 2021 Aug 3;S2050-0521(21)00040-8. doi: 10.1016/j.sxmr.2021.05.001.
https://pubmed.ncbi.nlm.nih.gov/34362711/

Introduction: Persistent genital arousal disorder (PGAD) is an uncommon condition resulting in intrusive, unwanted and distressing symptoms of genital arousal. Presentation can vary and most cases do not have an immediately identifiable etiology. Objectives: To present evaluation and treatment recommendations for PGAD from a multidisciplinary perspective and provide case examples.

Methods: A focused review of the literature on diagnosis, workup, and treatment of PGAD was completed. A case series of 3 varying presentations of PGAD is offered.

Results: PGAD results in high levels of patient distress and is best managed with a multidisciplinary treatment approach. Identification and management of co-occurring symptoms or disease states is imperative, particularly psychologic and psychiatric comorbidities. With appropriate intervention, patients may achieve improvement of their physical symptoms and a decrease in associated psychological distress. Conclusion: PGAD is an uncommon and highly distressing condition that requires thoughtful evaluation for appropriate diagnosis and treatment. Multidisciplinary treatment approaches provide the best opportunity to address the needs of patients and optimizing treatment response.

Pudendal Neuralgia

Therapeutic Efficacy of Ultrasound-Guided High-Voltage Long-Duration Pulsed Radiofrequency for Pudendal Neuralgia
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Neural Plast. 2021 Jul 30;2021:9961145. doi: 10.1155/2021/9961145. eCollection 2021.
https://pubmed.ncbi.nlm.nih.gov/34373690/

Pudendal neuralgia (PN) is a complex disease with various clinical characteristics, and there is no treatment showing definite effectiveness. This study is aimed at evaluating the clinical efficacy of ultrasound-guided high-voltage long-duration pulsed radiofrequency (PRF) for PN. Two cadavers (one male, one female) were dissected to provide evidence for localization of the pudendal nerve. Patients diagnosed as PN who failed or were intolerant in regular medication were screened for diagnostic local anesthesia block of the pudendal nerve before recruitment. Twenty PN patients were enrolled in this study. In the PRF procedure, the needle tip was inserted medially into the internal pudendal artery under ultrasound guidance. The position of the PRF needle tip was then adjusted by the response of the pudendal nerve to the electrical stimulation within the pudendal area (42°C, a series of 2 Hz, and 20 ms width pulses that lasted for 900 s). Alleviation of pain was assessed by the visual analogue scale (VAS) and sitting time pretreatment and on 7 d, 14 d, 1 m, 2 m, 3 m, and 6 m posttreatment in outpatient follow-up or by telephone interview. Two patients were lost due to intervention-irrelevant reasons. Patients showed significantly decreased VAS scores on 7 d after RFP, compared with pretreatment status (7.0 ± 0.9 vs. 3.2 ± 1.7, \( P < 0.001 \)). The efficacy remained steady till the end of 6 months, with a final remission rate of 88.9%. Sitting time also significantly lengthened following PRF (7 d, 14 d, 1 m, 2 m, 3 m, and 6 m vs. pretreatment, all \( P < 0.05 \)). Only short-term ipsilateral involuntary convulsion of the lower extremity was reported in one patient, who recovered within 12 h. Six patients were treated with nonsteroidal drugs for a short time. All patients stopped taking medication finally. In conclusion, the
ultrasound-guided high-voltage long-duration PRF approach not only reduced the pelvic pain caused by PN but also improved the quality of life by extending sitting time without nerve injury.

**Initial experience using a novel nerve stimulator for the management of pudendal neuralgia**
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Neurourology. 2021 Aug;40(6):1670-1677. doi: 10.1002/nau.24735. Epub 2021 Jun 30.
https://pubmed.ncbi.nlm.nih.gov/34196055/

**Aims:** In patients with pudendal neuralgia, prior studies have shown efficacy in chronic stimulation with Interstim® (Medtronic, Inc.). This feasibility study reports on the initial experience of using a wireless system to power an implanted lead at the pudendal nerve, StimWave®, to treat pudendal neuralgia.

**Methods:** Retrospective chart review identified patients with a lead placed at the pudendal nerve for neuralgia and powered wirelessly. Clinical outcomes were assessed at Postoperative visits and phone calls. Administered non-validated follow-up questionnaire evaluated the Global Response Assessment, percentage of pain improvement, satisfaction with device, and initial and current settings of the device (h/day of stimulation).

**Results:** Thirteen patients had the StimWave® lead placed at the pudendal nerve, 12 (92%) female and 1 (7.6%) male. Mean age was 50 years (range: 20-58). Failed prior therapies include medical therapy (100%), pelvic floor physical therapy (92%), pudendal nerve blocks (85%), pelvic floor muscle trigger point injections (69%), neuromodulation (30.7%), or surgeries for urogenital pain (23.1%). After the trial period, 10/13 (76.9%) had >50% improvement in pain with 6/13 (46.1%) reporting 100% pain improvement. Nine underwent permanent lead placement. At last postoperative visit (range, 6-83 days), 5/9 patients reported >50% pain improvement. Seven patients reached for phone calls (22-759 days) reported symptoms to be "markedly improved" (n = 2), "moderately improved" (n = 4), or "slightly improved" (n = 1). At follow up, complications included lead migration (n = 2), broken wire (n = 1), or nonfunctioning antenna (n = 2).

**Conclusion:** Complex patients with pudendal neuralgia may benefit from pudendal nerve stimulation via StimWave®.

**Lumbosacral plexus MR tractography: A novel diagnostic tool for extraspinal sciatica and pudendal neuralgia?**
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Magn Reson Imaging. 2021 Aug 14;83:107-113. doi: 10.1016/j.mri.2021.08.003.
https://pubmed.ncbi.nlm.nih.gov/34400289/

**Background:** Diagnosing extraspinal sciatica and pudendal neuralgia remains a clinical challenge. MRI and MR Neurography (MRN) are currently the standard techniques used to support the diagnosis of extraspinal lumbosacral plexus entrapments; however, for the intrapelvic portions of the lumbosacral plexus their accuracy is still limited. MR Tractography (MRT) feasibility to image the lumbosacral plexus has been demonstrated, but its clinical applications have yet to be determined. **Purpose:** To correlate MRT with intraoperative findings in patients undergoing laparoscopic treatment of intrapelvic entrapments of the lumbosacral plexus and compare its accuracy with Neuropelveological clinical assessment and MRN. **Materials and methods:** This is a retrospective analysis of MRT reconstructions of diffusion tensor imaging (DTI) sequences acquired for the MRN collected from a cohort of 13 patients undergoing laparoscopic detrapment of the lumbosacral plexus. The primary outcome of this study was the correlation of MRT reconstruction with intraoperative findings. Secondary outcomes included the correlation of MRN, preoperative Neuropelveological clinical diagnoses and the diffusion-weighted
imaging (DWI) fractional anisotropy (FA) and Apparent Diffusion Coefficient (ADC) in patients undergoing pelvic MRI and MRN for the investigation of intrapelvic nerve entrapments. **Results:** MRT correlated with intraoperative findings in 11 of 13 patients (85%). Neuropelveological clinical assessment was able to accurately diagnose a pelvic nerve entrapment in 12/13 patients (92%) and MRN agreed with surgical findings in only 2/13 (15%) patients. MRT was significantly superior to MRN (**p** < 0.001). FA and ADC did not correlate with the identification of a nerve entrapment, likely due to limitations regarding the placement of the seedpoints. **Conclusions:** This initial, retrospective analysis, suggests that MRT is superior to MRN at diagnosing intrapelvic entrapments of the lumbosacral plexus. A prospective, double-blinded study is underway to validate this data, but these initial findings show great potential for MRT as a diagnostic tool for extraspinal sciatica and pudendal neuralgia.

**Sexual dysfunction due to pudendal neuralgia: a systematic review**
Fouad Aoun, Marwan Alkassis, Georges Abi Tayeh, Josselin Abi Chebel, Albert Semaan, Julien Sarkis, Raymond Mansour, Georges Mjaess, Simone Albisinni, Fabienne Absil, Renaud Bollens, Thierry Roumeguère
Transl Androl Urol. 2021 Jun;10(6):2500-2511.doi: 10.21037/tau-21-13.
https://pubmed.ncbi.nlm.nih.gov/34295736/

**Background:** The pudendal nerve is considered as the main nerve of sexuality. Pudendal neuralgia is an underdiagnosed disease in clinical practice. The aim of this systematic review is to highlight the role of pudendal neuralgia on sexual dysfunction in both sexes. **Methods:** A PubMed search was performed using the following keywords: "Pudendal" AND "Sexual dysfunction" or "Erectile dysfunction" or "Ejaculation" or "Persistent sexual arousal" or "Dyspareunia" or "Vulvodynia". The search involved patients having sexual dysfunction due to pudendal neuralgia. Treatment received was also reported. **Results:** Five case series, seven cohort studies, two pilot studies, and three randomized clinical trials were included in this systematic review. Pudendal nerve and/or artery entrapment, or pudendal neuralgia, is a reversible cause of multiple sexual dysfunctions. Interventions such as anesthetic injections, neurolysis, and decompression are reported as potential treatment modalities. There are no studies describing the role of pudendal canal syndrome in the pathophysiology or treatment of delayed ejaculation or penile shortening. **Discussion:** Pudendal neuralgia is an underestimated yet important cause of persistent genital arousal, erectile dysfunction (ED), premature ejaculation (PE), ejaculation pain, and vulvodynia. Physicians should be aware of this entity and examine the pudendal canal in such patients before concluding an idiopathic cause of sexual dysfunction.

**Dermatological Conditions**

**Apremilast for genital erosive lichen planus in women (the AP-GELP Study): study protocol for a randomised placebo-controlled clinical trial**
Kristin Helene Skullerud, Petter Gjersvik, Are Hugo Pripp, Erik Qvigstad, Anne Lise Ording Helgesen Trials. 2021 Jul 20;22(1):469. doi: 10.1186/s13063-021-05428-w.
https://pubmed.ncbi.nlm.nih.gov/34284808/

**Background:** Genital erosive lichen planus (GELP) is a genital subtype of lichen planus, a chronic autoimmune inflammatory disease of unknown aetiology. In women, GELP is characterised by painful vulvo-vaginal mucosal erosions and scarring, often resulting in poor sexual health and reduced quality of
Treatment options are limited and often with little effect. Apremilast, a phosphodiesterase 4-inhibitor, has been shown to have a positive effect on psoriasis and other inflammatory skin diseases. We aim to investigate the effect and safety of peroral apremilast in women with GELP in a randomised placebo-controlled double-blinded clinical trial. **Methods:** We will recruit 42 adult women with characteristic clinical and/or histological features of moderate-to-severe GELP from a specialised vulva clinic in Oslo, Norway. The patients will be randomised 1:1 to either apremilast 30 mg BID (with an initial dose titration on days 1-6) or a placebo for 24 weeks. The concomitant use of topical corticosteroids will be allowed. The primary end point will be the mean GELP score, a clinical scoring system, at week 24 in the apremilast-treated patients versus the placebo-treated patients. The secondary end points will include the mean GELP score improvement from weeks 0 to 24, patient-reported use of topical steroids, the pain score on a visual analogue scale and the number of patients with GELP score improvements at weeks 16 and 24. The Physician Global Assessment, Patient Global Assessment and selected quality of life and sexual function assessments will be recorded at weeks 0, 16 and 24. The exploratory endpoints include description of immunohistochemical changes before and after apremilast therapy, assessed in vulvar or vaginal biopsies at weeks 0 and 24. Regular follow-ups for possible adverse events will be conducted. **Discussion:** The study design is based on experience from studies on apremilast in other inflammatory skin diseases using equivalent apremilast doses for approved indications. The trial may provide evidence for the use of apremilast in women with this burdensome genital dermatosis.

**Fractional CO2 laser and vulvar lichen sclerosus: an alternative resource during maintenance therapy? A prospective study**

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Ital J Dermatol Venerol. 2021 Jul 20. doi: 10.23736/S2784-8671.21.07066-3.

https://pubmed.ncbi.nlm.nih.gov/34282866/

**Background:** Lichen sclerosus is an autoimmune dermatosis that in women typically involves vulvar area. This condition can strongly impact on the quality of life. To date, topical steroids are the most effective treatment, although adverse effects are possible, especially in long-term application. The aim of this study is to investigate the efficacy of fractional CO2 laser in reducing symptoms of vulvar lichen sclerosus (VLS) during maintenance therapy with topical steroids (application twice weekly or less);(ii) to assess how long this reduction of symptoms persists during followup; (iii) histological comparison before and after treatment. To our knowledge, this is the first prospective study evaluating this treatment in women with VLS. **Methods:** Women with a diagnosis of VLS were prospectively enrolled and treated with fractional CO2 laser every 2 months, for a total of 3 sessions. Four questionnaires were periodically administered: the Dermatology Quality of Life Index (DLQI), the Female Sexual Functional Index (FSFI) and 2 specific questionnaires created to assess the severity of disease. **Results:** 23 adult women were enrolled. The fractional CO2 laser treatment significantly improved the scores of all scales from baseline to T4 questionnaires. **Conclusions:** Fractional CO2 laser proved to be effective on VLS symptoms and can be considered an alternative to corticosteroids during maintenance therapy. Larger studies with a control group and randomization are needed to safely generalize our findings.
Human beta defensin levels and vaginal microbiome composition in post-menopausal women diagnosed with lichen sclerosus
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Sci Rep. 2021 Aug 6;11(1):15999.doi: 10.1038/s41598-021-94880-4. https://pubmed.ncbi.nlm.nih.gov/34362937/

Human beta defensins (hBDs) may play an important role in the progression of lichen sclerosus (LS), due to their ability to induce excessive stimulation of extracellular matrix synthesis and fibroblast activation. The genetic ability of the individual to produce defensins, the presence of microbes influencing defensin production, and the sensitivity of microbes to defensins together regulate the formation of an ever-changing balance between defensin levels and microbiome composition. We investigated the potential differences in postmenopausal vaginal microbiome composition and vaginal hBD levels in LS patients compared to non-LS controls. LS patients exhibited significantly lower levels of hBD1 (p = 0.0003), and significantly higher levels of hBD2 (p = 0.0359) and hBD3 (p = 0.0002), compared to the control group. The microbiome of the LS patients was dominated by possibly harmful bacteria including Lactobacillus iners, Streptococcus anginosus or Gardnerella vaginalis known to initiate direct or indirect damage by increasing defensin level production. Our observations highlight that correcting the composition of the microbiome may be applicable in supplementary LS therapy by targeting the restoration of the beneficial flora that does not increase hBD2-3 production.

Vulvar Lichen Sclerosis from Pathophysiology to Therapeutic Approaches: Evidence and Prospects
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Biomedicines. 2021 Aug 3;9(8):950. doi: 10.3390/biomedicines9080950. https://pubmed.ncbi.nlm.nih.gov/34440154/

Vulvar lichen sclerosus (VLS) is a chronic, distressing, inflammatory disease with an enormous impact on quality of life. Treatment goals are relieving symptoms, reversing signs and preventing anatomical changes. Despite the availability of numerous therapeutic options, treatment outcome may not be entirely satisfactory and a definitive cure does not exist. This may be due to the fact that the exact VLS etiopathogenesis remains unknown. The objectives of this paper were to review the most up-to-date knowledge on VLS etiopathogenesis and to consider the available therapies through the lens of a plausible pathogenetic model. An electronic search on both VLS etiopathogenesis and its treatment was performed using the National Library of Medicine PubMed database. Based on current knowledge, it is conceivable that various, heterogeneous environmental factors acting on a genetic background trigger an autoimmune, Th-1 response, which leads to a chronic inflammatory state. This, in turn, can determine both tissue and micro-vascular injury and activation of signaling pathways involved in fibroblast and collagen metabolism. This pathogenetic sequence may explain the effectiveness of anti-inflammatory treatments, mostly topical corticosteroids, in improving VLS clinical-pathological changes. Further deepening of the disease pathways will presumably allow key mediators to become new therapeutic targets and optimize the available treatments.
Topical Corticosteroids in the Treatment of Vulvar Lichen Sclerosus: A Review of Pharmacokinetics and Recommended Dosing Frequencies
Theodora T Mautz, Jill M Krapf, Andrew T Goldstein
Sex Med Rev. 2021 Jul 2;S2050-0521(21)00033-0. doi: 10.1016/j.sxmr.2021.03.006.
https://pubmed.ncbi.nlm.nih.gov/34226161/

Topical corticosteroids are often utilized as the first-line treatment for vulvar lichen sclerosus (VLS). However, there is wide variability in dosing regimens, as well as a lack of consensus on maintenance dosing. Available guidelines on dosing frequency and regimen continuation for VLS are based on clinical expert opinion and do not necessarily reflect the pharmacokinetics of topical corticosteroids. Over the past few decades, there have been many advances in the techniques used to measure the local and systemic absorption of topical corticosteroids. These techniques have led to a greater understanding of the pharmacokinetics and bioavailabilities of these medications. However, it is not clear how this new information has been applied in evaluating dosing regimens and commonly cited risks when considering short- and long-term use in different vulvar dermatoses. This purpose of this review is to evaluate the available evidence on pharmacokinetics, absorption rates, and concentration levels of topical corticosteroids in lesional and nonlesional skin. Additionally, the evidence regarding commonly cited risks of topical corticosteroid use, including dermal thinning, adrenal suppression, systemic immunosuppression, and tachyphylaxis are reviewed. Differences in the effects of topical corticosteroids on the varied tissues of the vulva are specifically explored. Finally, these considerations are applied to evaluate the current treatment guidelines for VLS to provide direction in determining an evidenced-based dosing regimen and to inform future research in this area. Mautz TT, Krapf JM, Goldstein AT.

Treatment with Theresienöl - a new option in the management of vulvar leukoplakia
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Prz Menopauzalny. 2021 Jun;20(2):72-75. doi: 10.5114/pm.2021.106220. Epub 2021 May 24.
https://pubmed.ncbi.nlm.nih.gov/34321984/

Introduction: The term vulvar leukoplakia encompasses a variety of non-inflammatory diseases that lead to skin discoloration of the external genitalia and white colouration. Most commonly, these are vulvar lichen sclerosus (VLS) and squamous cell hyperplasia of the vulva (SCHV). They have similar aetiology, clinical presentation, and treatment but different anatomical pathology. Aim of the study: The study aims to determine the effect of Theresienöl herbal oil treatment in patients with clinically proven diagnosis of VLS and SCHV. Material and methods: This prospective study includes 17 patients with a diagnosis of VLS and SCHV, who underwent a 3-month treatment course with Theresienöl herbal oil. All patients were followed up for 1 year after therapy initiation, and the effect of treatment was reported using a visual analogue scale (VAS) for genital itching. Results: The median age of patients enrolled was 60.6 years (range 42-74); 2 patients dropped out due to failure to attend follow-up visits. The mean score of the VAS taken at the beginning of treatment was 1.65 (0-5); at the 3rd month the mean score was 9 (8-10) and it remained similar at the 12th month - 8.67 (7-10). Conclusions: Theresienöl herbal oil treatment of vulvar leukoplakia is effective and safe, but studies should be continued.
Lichen sclerosus of the vulva
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Climacteric. 2021 Jul 27;1-8. doi: 10.1080/13697137.2021.1948004.
https://pubmed.ncbi.nlm.nih.gov/34313164/

Lichen sclerosus of the vulva (LSV) is seen frequently enough to warrant knowing how to diagnose it and institute appropriate treatment strategies. LSV is a chronic skin disorder, very likely of autoimmune origin, which may affect various areas of the perineum, although some women may be affected in extragenital areas. The disease has significant adverse impact on quality of life and sexual activity and may undergo malignant transformation. History of symptomatology and clinical examination is sufficient to make the diagnosis. Skin biopsy is only necessary in specific scenarios. Topical corticosteroids are still the mainstay of therapy, initially to institute remission and then for maintenance. Long-term therapy and surveillance are invariably necessary. Surgery does have a role, but only in specific associated conditions. A number of alternative treatment options have been mooted, especially if the disease is resistant to topical corticosteroids, but these options are still being assessed and studied.

Lichen Sclerosus
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In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. 2021 Jul 18.
https://pubmed.ncbi.nlm.nih.gov/30855834/

Lichen sclerosus (LS) is a chronic inflammatory disease. It was first described by Hallopeau in 1881. Since then, multiple names have been used to describe this condition such as leukoplakia, kraurosis vulvae, balanitis xerotica obliterans, and lichen sclerosis et atrophicus. In 1976, the International Society for the Study of Vulvovaginal Disease adopted the term of lichen sclerosus.
LS is a mucocutaneous autoimmune disorder characterized by hypopigmentation and skin atrophy. It involves most commonly the genital skin, less often the extragenital sites. LS is more common in women than in men. It may cause phimosis or scarring of the vaginal introitus. The diagnosis is based on the clinical features, but it is often confirmed by biopsy. The lesions can evolve towards the destruction of anatomic structures, functional impairment and a potential risk for malignant evolution. Thus, treatment and long term follow-up are mandatory.

Erosive vulvo-vaginal lichen planus treated with rituximab: A case report
Maria Lagerstedt, Laura Kotaniemi-Talonen, Jaakko Antonen, Annikki Vaalasti
Int J Gynaecol Obstet. 2021 Jul 2. doi: 10.1002/ijgo.13814.
https://pubmed.ncbi.nlm.nih.gov/34214191/
https://www.researchgate.net/publication/352928032_Erosive_vulvo-vaginal_lichen_planus_treated_with_rituximab_A_case_report

Erosive lichen planus (ELP) is a variant of lichen planus that affects the mucosal membranes of the vulva, vagina, oral cavity, and, in rare cases, the esophagus or urethra [1]. ELP is characterized by a chronic and relapsing course. The inflammatory reaction in ELP is mainly T cell–mediated, leading to keratinocyte apoptosis in the basal layer of the epidermis; however, a humoral mechanism may also be included.
Background: Lichen sclerosus (LS) affects the female anogenital area, causing anatomical changes. Reported symptoms include itching, soreness and dyspareunia. **Objective:** This cross-sectional study intends to evaluate the quality of life and sexual functioning in women with LS. **Methods:** 158 women aged over 18, diagnosed with LS, and referred to North Denmark Regional Hospital from January 2018 to November 2019 were included. The questionnaires 'Female Sexual Function Index (FSFI)', 'Dermatology Life Quality Index (DLQI)', and the 'WHO-5 Well-Being Index' were completed. **Results:** The women (mean age 47 years (18-76)) presented a low score on all FSFI scales, with a mean score of 13.83 (95% CI: 12.46;15.20), indicating reduced sexual functioning. The sub-group evaluation scored as follows: Desire 2.32; arousal 2.23; lubrication 2.39; orgasm 2.28; satisfaction 3.02; pain 1.59. The results from DLQI revealed a mean score of 7.88 (95% CI: 7.02;8.74), indicating a moderate effect on the women´s everyday life. The mean sub-scores were: Treatment 0.32; sexual difficulties 1.56; relations 1.02; work/study 0.34; sport 0.45; social activities 0.54; clothing 0.89; shopping 0.22; embarrassment 0.99 and itching, soreness and, pain 1.55. The mean score for the WHO-5 Well-Being Index was 56.66 (95% CI: 53.48;59.84) indicating that 40% of the women had signs of depression. **Conclusions:** This study concludes that LS has a considerable influence on the sexual functioning and quality of life of women. Health care professionals must not only consider the biological aspects but also the psychological and social aspects.