Vulvodynia: A disease commonly hidden in plain sight.

Vulvodynia affects at least 6% of women, and can be found at any age and in all ethnic groups. The diagnosis is one of exclusion but is very often missed. Women with vulvodynia are frequently misdiagnosed as having vaginismus. Failure to make the diagnosis often leads to irrelevant or deleterious examinations and treatments.

Vulvodynia in adolescents: presentation, diagnosis and treatment options.
Hersh JE

PURPOSE OF REVIEW: Vulvodynia in adults is a significant source of genital and sexual pain with far reaching negative repercussions. Well designed studies with sufficient power in adults are limited and there are even fewer in adolescents. This review will help the clinician understand, diagnose and treat vulvodynia in adolescents based on current knowledge. RECENT FINDINGS: Although research on vulvodynia in adolescents is lacking, studies suggest that it not only exists but also may negatively impact an adolescent’s medical and sexual health. This review will look at both historical approaches to vulvodynia, as well as more current approaches. It is important to note that no treatment modalities have been specifically approved for use in vulvodynia. SUMMARY: Vulvodynia in women is known to have significant impact on general health and sexual wellbeing. How early vulvodynia presents is unknown, but it appears that in at least some cases, it can be found in adolescents. Providers of
adolescent care should have knowledge of this pain disorder so that they may appropriately diagnose and manage this multifactorial problem.

**Effectiveness of two different acupuncture strategies in patients with vulvodynia: Study protocol for a pilot pragmatic controlled trial.**

**BACKGROUND:** Vulvodynia, or vulvar pain, is a common condition in women; however, there are few evidence-based clinical trials evaluating nonpharmacological therapies for this condition. Acupuncture is one complementary and integrative medicine therapy used by some patients with vulvodynia. This study evaluates two different acupuncture strategies for the treatment of vulvodynia and aims to evaluate whether either of the acupuncture protocols reduces vulvar pain, pain duration or pain with intercourse. The study also examines how long the effect of acupuncture lasts in women with vulvodynia.

**METHODS/DESIGN:** The study is designed as a randomized controlled trial, focused on two acupuncture protocols. Fifty-one patients who have had vulvodynia for more than 3 months will be recruited. Among them, 34 patients will be randomized into Groups 1a and 1b; those who are unwilling to receive acupuncture will be recruited into the standard care group (Group 2). Patients in Group 1a will have acupuncture focused on the points in the pudendal nerve distribution area, while patients in Group 1b will receive acupuncture focused on traditional (distal) meridian points. Patients in Group 2 will receive routine conventional treatments, such as using pain medications, local injections and physical therapies or other nonsurgical procedures. Acupuncture will last 45 min per session, once or twice a week for 6 weeks. The primary outcome measurement will be objective pain intensity, using the cotton swab test. The secondary outcome measurement will be subjective patient self-reported pain intensity, which will be conducted before cotton swab test. Pain intensities will be measured by an 11-point Numeric Pain Rating Scale. Pain duration and pain score during intercourse are recorded. Local muscle tension, tenderness and trigger points (Ashi points) are also recorded. All measurements will be recorded at baseline (before the treatment), at the end of each week during treatment and at the end of the 6 weeks. Follow-up will be done 6 weeks following the last treatment.

**DISCUSSION:** Results of this trial will provide preliminary data on whether acupuncture provides better outcomes than nonacupuncture treatments, i.e., standard care, and whether acupuncture focused on the points in pudendal nerve distribution, near the pain area, has better results than traditional acupuncture focused on distal meridian points for vulvodynia.

**The Vulvar Vernacular: Dilemmas Experienced and Strategies Recommended by Women with Chronic Genital Pain.**
Hintz EA.

This manuscript uses Goldsmith's (2004) normative model of social support to explore conversations women have with a romantic partner about vulvodynia. Twenty-six women with vulvodynia participated in semi-structured interviews in which they described conversational goals, discussed challenges, and offered advice to others managing vulvodynia. As this study was concerned with interactions with romantic partners both present and past, women with vulvodynia, not their partners, were the targets.
of recruiting efforts. Two key communicative dilemmas emerged from the data analysis: (a) I need to talk to you, but I can't, and (b) I want to be honest, but not too honest. These dilemmas represent ambiguity about the causes and duration of pain and the implications that being unable to have pain-free intercourse has for their relationships and identities as women. Three strategies, communicative practices for managing dilemmas, also emerged: (a) reframe the illness, (b) refocus the relationship, and (c) redefine intimacy. The theoretical and practical implications of this research are socially situated within timely conversation about women, their bodies, and their roles.

**Provoked Vestibulodynia**

Localized Provoked Vulvodynia: Association With Nerve Growth Factor and Transient Receptor Potential Vanilloid Type 1 Genes Polymorphisms.

**OBJECTIVE:** The aim of the study was to study the associations between localized provoked vulvodynia (LPV) and several single-nucleotide polymorphisms (SNPs) in the transient receptor potential vanilloid type 1 (TRPV1), nerve growth factor (NGF), and the heparanase (HPSE) genes. **MATERIALS AND METHODS:** Prevalence of SNPs among 65 women with moderate or severe primary LPV (initial symptoms occur with first provoking physical contact) and 126 healthy, ethnically matched controls was analyzed in an observational case-control study. Each participant answered a questionnaire addressing familial LPV occurrence and comorbid pain conditions. **RESULTS:** Familial occurrences of LPV, temporomandibular joint (TMJ) symptoms, recurrent vaginitis, and irritable bowel syndrome were significantly higher among LPV women than healthy controls. Genotyping analyses revealed a novel, statistically significant high prevalence of polymorphism c.945G>C (rs222747) of TRPV1 and a SNP in the promoter region of NGF (rs11102930) in LPV women compared with controls. A logistic regression model for rs222747 and rs11102930 frequent alleles indicates significant LPV association within the entire study group and Ashkenazi Jewish women, respectively. Comparison of pain conditions with frequent alleles showed the rs222747 "CC" genotype of TRPV1 associated with women with TMJ, recurrent vaginitis, and LPV. **CONCLUSIONS:** Our results suggest novel genetic susceptibility to primary LPV associated with specific alleles in genes TRPV1 and NGF and propose the rs222747 "C" allele of TRPV1 as a common genetic predisposition for other pain syndromes.

Effect of gabapentin on sexual function in vulvodynia: a randomized, placebo-controlled trial.

**BACKGROUND:** Sexual dysfunction is common in women with vulvodynia. **OBJECTIVE:** The purpose of this study was (1) to evaluate whether extended-release gabapentin is more effective than placebo in improving sexual function in women with provoked vulvodynia and whether there is a relationship between treatment outcome and pelvic pain muscle severity that is evaluated by palpation with standardized applied pressure and (2) to evaluate whether sexual function in women with provoked
vulvodynia would approach that of control subjects who report no vulvar pain either before or after treatment. **STUDY DESIGN:** As a secondary outcome in a multicenter double-blind, randomized crossover trial, sexual function that was measured by the Female Sexual Function Index was evaluated with gabapentin (1200–3000 mg/d) compared with placebo. Pain-free control subjects, matched by age and race, also completed Female Sexual Function Index for comparison. **RESULTS:** From August 2012 to January 2016, 230 women were screened at 3 academic institutions, and 89 women were assigned randomly to treatment. Gabapentin was more effective than placebo in improving overall sexual function (adjusted mean difference, 1.3; 95% confidence interval, 0.4–2.2; P = .008), which included desire (mean difference, 0.2; 95% confidence interval, 0.0–3.3; P = .04), arousal (mean difference, 0.3; 95% confidence interval, 0.1–0.5; P = .004), and satisfaction (mean difference, 0.3; 95% confidence interval, 0.04–0.5; P = .02); however, sexual function remained significantly lower than in 56 matched vulvodynia pain-free control subjects. There was a moderate treatment effect among participants with baseline pelvic muscle pain severity scores above the median on the full Female Sexual Function Index scale (mean difference, 1.6; 95% confidence interval, 0.3–2.8; P = .02) and arousal (mean difference, 0.3; 95% confidence interval, 0.1–0.6; P = .01) and pain domains (mean difference, 0.4; 95% confidence interval, 0.02–0.9; P = .04). **CONCLUSION:** Gabapentin improved sexual function in this group of women with provoked vulvodynia, although overall sexual function remained lower than women without the disorder. The most statistically significant increase was in the arousal domain of the Female Sexual Function Index that suggested a central mechanism of response. Women with median algometer pain scores >5 improved sexual function overall, but the improvement was more frequent than the pain domain. We hypothesize that gabapentin may be effective as a pharmacologic treatment for those women with provoked vulvodynia and increased pelvic muscle pain on examination.
Candida in vitro. **RESULTS:** We included a total of 14 studies, both population and clinic-based case-control, and pathophysiological research. 7 studies were of low methodological quality, and 7 studies were of medium methodological quality. The population-based case-control studies showed a significantly increased odds ratio for self-reported VVC in PVD cases compared with controls. The pathophysiological studies revealed a tendency for an increased local proinflammatory response on Candida in vitro in patients with PVD. Owing to the substantial heterogeneity of the studies, meta-analysis was not performed. **CLINICAL IMPLICATIONS:** Health care providers may consider a diagnosis of PVD in women with self-reported VVC, and to act on this properly. Reiteration of antifungal prescriptions by physicians without a decent diagnosis, will lead to mistreatment. Women should be informed by their health care provider that intercourse during (or shortly after) the treatment of VVC might worsen the vulnerability of the vulvar skin. **STRENGTH AND LIMITATIONS:** This is the first systematic review performed to describe the relation between VVC and PVD. An independently performed in- and exclusion process and quality appraisal, ensured optimal internal validity. However, there were important methodological limitations and the size of heterogeneity prevented establishing a meta-analysis. **CONCLUSION:** This systematic review is unable to draw conclusions regarding a relationship between actual VVC and PVD because studies were based on self-reported VVC. Until new evidence becomes available, we advocate that PVD should be considered as an unexplained chronic pain condition. In women with recurrent or persistent VVC-like complaints, physicians should consider a diagnosis of PVD.

**Outcome Measurement Instruments for Provoked Vulvodynia: A Systematic Review.**

Davenport RB, Voutier CR, Veysey EC.


**OBJECTIVE:** The objective of this study was to detail the outcome measurement instruments used in randomized control trials and observational studies investigating therapeutic interventions for provoked vulvodynia. **MATERIALS AND METHODS:** We searched Ovid Medline, Embase, Emcare, and PyschINFO libraries from database inception through April 2017. We included randomized control trials and observational studies of provoked vulvodynia that used instruments to measure the outcome of therapeutic interventions. **RESULTS:** A total of 2299 articles were retrieved and 25 were eligible for inclusion in accordance with the selection criteria. The included studies measured 26 different outcomes, using 110 outcome measurement instruments. Patient-reported outcomes were most commonly measured (144/166, 86%), followed by physician-reported outcomes (20/166, 12%). The most commonly measured outcomes were patient-reported psychological impact of disease (27/166, 16%), patient-reported improvement in dyspareunia (25/166, 15%), and patient-reported reduction in pain (24/166, 14%). The Pain Catastrophizing Scale, the Beck Depression Inventory, and the State Trait Anxiety Questionnaire were the most commonly used instruments to measure psychological impact. The most commonly measured clinician-rated outcome was an improvement in pain (17/166, 10%), which was most frequently assessed by the cotton swab test. Only 34 (31%) outcome measurement instruments were specific to vulvodynia (26/110, 23%) or sexual functioning (8/110, 7%). **CONCLUSIONS:** There is a wide range of outcome measurement instruments used in provoked vulvodynia studies, resulting in inconsistency of reporting and difficulty in comparing and combining findings for systemic review. There is a pressing need for the development of validated, reliable instruments and consensus on a core outcome set for further research purposes.

Glowacka M, Bergeron S, Delisle I, Rosen NO.

Provoked vestibulodynia (PVD), a common cause of women's genitopelvic pain, is associated with poorer psychological and sexual well-being in affected couples. Greater sexual contingent self-worth (CSW)-defined as self-esteem that is dependent on the perceived success or failure of a sexual relationship-has been linked to poorer well-being in a cross-sectional study of couples coping with PVD. This study aimed to examine whether daily sexual distress mediated the associations between greater sexual CSW and lower sexual satisfaction and greater anxiety, depressed mood, and women's pain in affected couples. Women (N = 125) diagnosed with PVD and their partners completed the Sexual CSW Scale and then online daily surveys for eight weeks measuring sexual distress, sexual satisfaction, anxiety, depressed mood, and women's pain during intercourse. Multilevel analyses were based on the actor-partner interdependence model (APIM). For women who had higher sexual CSW (compared to lower sexual CSW), on sexual activity days when their sexual distress was higher, they reported lower sexual satisfaction and greater anxiety, depressed mood, and pain (compared to their average level across all sexual activity days). Findings suggest that daily sexual distress may be one pathway between greater sexual CSW and poorer day-to-day well-being in women with PVD.

Co-morbid Disorders

Female Genito-Pelvic Pain/Penetration Disorder: Review of the Related Factors and Overall Approach.
Dias-Amaral A, Marques-Pinto A.

Genito-pelvic pain/penetration disorder (GPPPD) can be an extremely bothersome condition for patients, and a tough challenge for professionals regarding its assessment and treatment. The goal of the present paper is to review the etiology, assessment, and treatment of GPPPD, especially focusing on the cognitive aspects of the disease and cognitive-behavioral treatment options, through a non-systematic review of articles indexed to the Medline, Scopus and Web of Science databases, using the following MeSH queries: pelvic pain; dyspareunia; vaginismus; vulvodynia; and cognitive therapy. Altogether, 36 articles discussing the etiology, diagnosis and management of GPPPD were selected. We provide an overview of GPPPD based on biological, psychological and relational factors, emphasizing the last two. We also summarize the available medical treatments and provide strategies to approach the psychological trigger and persisting factors for the patient and the partner. Professionals should be familiarized with the factors underlining the problem, and should be able to provide helpful suggestions to guide the couple out of the GPPPD fear-avoidance circle.
Pelvic pain is common in both reproductive age and postmenopausal women, and the major etiologies change throughout the life cycle. Chronic pain is defined as lasting for at least 6 months. There are many gastrointestinal and urinary disorders associated with chronic pain in this age group, which are not discussed in this guideline. Pain may be localized to the deep pelvis, with potential causes including pelvic congestion syndrome, intraperitoneal adhesions, hydrosalpinx, chronic inflammatory disease, or cervical stenosis. Ultrasound is the initial imaging modality of choice, while CT and MRI may be appropriate for further characterization of sonographic findings. Alternatively, pain may be localized to the vagina, vulva, or perineum, with potential causes including vaginal atrophy, vaginismus, vaginal or vulvar cysts, vulvodynia, or pelvic myofascial pain. Imaging is primarily indicated in context of an abnormal physical exam and ultrasound is the initial modality of choice, while MRI may be appropriate for further characterization in select cases. The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.


Background: The vulvovestibular syndrome (VVS) is a chronic, inflammatory, multifactorial, chronic inflammation of the female urogenital access. Methods: The aim of this anecdotal, observational, retrospective, case-control study was to comparatively evaluate the most common bacterial strains (Lactobacillus spp., Klebsiella spp., Gardnerella spp., and Streptococcus spp.) and fungi (Candida spp., Penicillium spp., and Aspergillus spp.) in vulvodinic women, and in women without gynecological symptoms (control group). Results: We found that vulvodinic patients had statistically lower Lactobacilli and higher total Fungi concentration. Conclusions: Our preliminary study is useful to further clarify the etiopathology of vulvodynia and suggest new therapeutic strategies for approaching the VVS.

The clinical anatomy of dyspareunia: A review.
Alimi Y, Iwanaga J, Oskouian RJ, Loukas M, Tubbs RS.

Dyspareunia can be described as continuous unremitting or intermittent pain associated with intercourse. It can be classified based on the location of the pain - entry or deep dyspareunia, or based
on when the pain was first experienced - primary or secondary dyspareunia. There are different causes of dyspareunia and some of the most important causes include the following: vulvodynia, postpartum dyspareunia, endometriosis, inadequate vaginal lubrication or arousal, and other anogenital causes such as hemorrhoids and anal fissures. In this review, our objective is to apply the anatomical knowledge of dyspareunia to patient care, increase awareness among clinicians about the diverse etiology of dyspareunia and ensure that the whole patient, not just the pain of dyspareunia is being treated as the causes of dyspareunia can be due to various pathologies.

**Pudendal Neuralgia**

**Clinical effect and safety of pulsed radiofrequency treatment for pudendal neuralgia: a prospective, randomized controlled clinical trial.**

**Background:** Pudendal neuralgia is an intractable pain related to the pudendal nerve. The clinical effect and safety evaluation of pudendal neuralgia were investigated by pulse radiofrequency (PRF) treatment of pudendal nerve. **Patients and methods:** Eighty patients who were diagnosed with pudendal neuralgia were randomly divided into PRF group (PRF and pudendal nerve block [NB]) and NB group. After surgery, the patients were followed up to evaluate the visual analog scale (VAS) score and the Patient Health Questionnaire score on the postoperative day and at 2 weeks, 1 and 3 months. Meanwhile, the patients’ efficacy assessment and the usage of pain medication were also recorded for 3 months during follow-up. All the surgical complications were recorded. **Results:** A total of 77 patients were followed up, 38 in the PRF group and 39 in the NB group. On the postoperative day, the VAS scores was significantly decreased in both groups than before (P<0.01), whereas there was no statistical difference within the two groups (P>0.05). However, the VAS score of PRF group was significantly lower than that of NB group in 2 weeks, 1 and 3 months after surgery, respectively (P<0.01). In the meanwhile, the Patient Health Questionnaire score of PRF group was also significantly lower than that of NB group (P<0.01) in 3 months after the operation. The clinical effective rate of PRF group was 92.1% in 3 months after surgery, while this rate was only 35.9% in the NB group. The postoperative analgesic usage of PRF group was superior to that of NB group (P<0.01). No severe adverse events were observed in either group. **Conclusion:** Compared with the single NB treatment, pudendal nerve PRF combined with NB therapy could provide more long-lasting relief from pain symptoms of pudendal neuralgia and improve the depression symptoms in patients.

**The drug-resistant pudendal neuralgia management: A systematic review.**
Tricard T, Munier P, Story F, Lang H, Saussine C.

**AIMS:** Pudendal neuralgia (PN) due to pudendal nerve entrapment is a well-known disease in medical community but both diagnostic and treatment may be delayed for patients. The goal of this study was to achieve a systematic review of the published treatments of PN in order to help physician to take their decision to treat PN. **METHODS:** A Systematic review based on MEDLINE, Embase, and Cochrane
databases was performed to identify articles related to PN. Studies involving ≥ 10 patients presenting PN according to Nantes's criteria who were managed with an intervention for their pain were reviewed. Data were extracted manually for qualitative analysis. **RESULTS:** Fifteen studies involving 672 patients (mean age 53.2 +/-5.1, SD 95%) were included. Nine different types of treatments were evaluated. Effectiveness of the treatments was heterogeneously assessed. Pain improvement was achieved in 41% to 100%, 13.4% to 100%, 60% to 100%, 12.2% to 100% in immediate, 3-month, 6-month, and 1-year post procedure, respectively. Complications reported were all grade ≤ II of Dindo-Clavien classification's. Given the heterogeneity of the outcomes measures and the lack of homogeneous prospective studies, no recommendation could be established to choose in between treatments. Methodological quality of the studies was heterogeneous. **CONCLUSION:** Many treatments seems available for drug-resistant PN. Given the heterogeneity of the outcomes measures and the lack of homogeneous prospective studies, no recommendation could be established to determine the best management strategy. Further studies about PN management are needed and should have common endpoint and follow-up.

**Tacrolimus 0.03% ointment for treatment of paediatric lichen sclerosus: a case series and literature review.**
Mazzilli S, Diluvio L, Di Prete M, Rossi P, Orlandi A, Bianchi L, Campione E.

Objectives This study aimed to investigate the usefulness and tolerability of topical tacrolimus in paediatric vulvar lichen sclerosus (LS). We examined whether there was improvement of the most problematic symptoms, such as itching, pain, and vulvar constipation. Methods Ten girls, aged from 4 to 9 years old who were affected by vulvar LS, were enrolled in an open clinical study to confirm the efficacy of tacrolimus 0.03% ointment to treat LS. Tacrolimus was applied twice a day for 6 weeks and then stopped during the follow-up period. The study duration included 6 weeks of treatment and 6 weeks of follow-up. A literature search of the PubMed (MEDLINE) database was conducted of reports published since 1 January, 2004. Results Our study and previous studies indicated the potential effectiveness of tacrolimus in LS. Treatment with topical tacrolimus was well tolerated with significant improvement of itching, pain, and constipation. Conclusion Tacrolimus may be a safe and effective alternative treatment, without the risk of corticosteroid-related vulvar atrophy, for paediatric vulvar LS. LS could become a further indication of topical tacrolimus therapy if these promising results are confirmed in the future.

**Combining topical tretinoin with mometasone furoate in the treatment of vulvar lichen sclerosus: Results of dermoscopic assessment.**
Corazza M, Maietti E, Toni G, Virgili A, Borghi A.

The main purpose of the present study was to compare the dermoscopic changes on vulvar lichen sclerosus (VLS) induced by two different 12-week treatment protocols, namely mometasone furoate 0.1% ointment plus tretinoin 0.05% cream in short-contact therapy (group A) versus the same
corticosteroid plus emollient (group B). All dermoscopic images captured before and after treatment were assessed. Each dermoscopic variable selected for the study purpose was arbitrarily graded according to a 4-point scale by dermatologists blinded to both the time at which the images were captured and treatment allocation. Seventeen patients in group A and 15 in group B were included. The vessel mean dermoscopic scores increased significantly after treatment, whereas the scores of (a) patchy, structure-less, whitish areas, (b) whitish background, (c) comedo-like openings, and (d) purpuric blotches decreased. At the control visit, the two protocols did not differ significantly for any of the dermoscopic parameters, both in terms of mean score change and in the number of patients showing changes. Although the complementary action of the two molecules may suggest a therapeutic benefit, the association of tretinoin in short contact therapy with a potent corticosteroid did not induce significant changes in the dermoscopic features of VLS compared with the same corticosteroid alone.

Extragenital lichen sclerosus successfully treated with narrowband-UVB phototherapy.
Motegi SI, Sekiguchi A, Fujiwara C, Yamazaki S, Ishikawa O.

Fact or Fiction? Adipose-Derived Stem Cells and Platelet-Rich Plasma for the Treatment of Vulvar Lichen Sclerosis.
Eshtiaghi P, Sadownik LA.

OBJECTIVE: The aim of the study was to summarize and review the evidence for the efficacy and safety of adipose-derived stem cells (ADSCs) and platelet-rich plasma (PRP) for the treatment of vulvar lichen sclerosus (LS). MATERIALS AND METHODS: PubMed/MEDLINE, Ovid, Web of Science, and clinicaltrials.gov were searched from inception up to May 7, 2018. RESULTS: Seven observational studies were identified, with a total of 98 patients. Both ADSCs and PRP were reported to improve symptoms, quality of life measures, as well as clinical and histological signs of vulvar LS. There is a strong risk of biased estimates of treatment effect. CONCLUSIONS: Current evidence is weak for ADSCs and/or PRP as treatment for vulvar LS. Further research is needed before recommending this therapy.

Cushing syndrome induced by topical corticosteroids for the treatment of lichen sclerosus.
Notay M, Fazel N, Awasthi S.

BACKGROUND: Lichen sclerosus is a chronic inflammatory dermatological condition with a predilection for the anogenital area. CASE: We describe a case of iatrogenic Cushing syndrome from the administration of high potency topical steroids for vulvar lichen sclerosus in a six-year-old girl. Her symptoms resolved after the cessation of topical steroids. SUMMARY AND CONCLUSION: This case brings attention to iatrogenic Cushing syndrome as a potential complication when using high potency topical corticosteroids in the anogenital region.
Vulvar lichen sclerosus in a prepubertal girl.
Rodrigues A, Cabral AJ, Faria A, Marques A.