

Improving women's lives through education, research, support and advocacy

Research Update E- Newsletter December 2022 – January – February 2023 www.nva.org

#### Vulvodynia

# Treating where it hurts-a randomized comparative trial of vestibule estradiol for postmenopausal dyspareunia

Martha F Goetsch, Bharti Garg, Jen Lillemon, Amanda L Clark Menopause. 2023 Feb 14. doi: 10.1097/GME.000000000002162. https://pubmed.ncbi.nlm.nih.gov/36787525/

**Objective:** To compare efficacies of two strengths of estradiol cream applied to the vulvar vestibule and use of silicone lubricant to reduce intercourse pain scores in postmenopausal women with moderate/severe dyspareunia. Methods: This pilot randomized comparative trial assigned 50 women to nightly applications of estradiol cream, 50 or 100 µg, for 12 weeks. We asked women to have lubricated penetration twice weekly, with intercourse or performing a tampon test. Pain, recorded in dairies, was rated using the 0-10 Numerical Rating Scale. We assessed biopsychosocial outcomes, urinary symptoms, and measured serum estradiol levels and endometrial stripe thicknesses. We performed physical examinations to determine tenderness levels of the vestibule, vagina, pelvic floor muscles, bladder, uterus, and adnexa. Comparisons were made using two-sample t test, Wilcoxon rank-sum test, or  $\chi^2$ /Fisher's exact test. **Results:** Forty-seven women (94%), with a mean age of 59.7 years, completed the trial. The baseline median intercourse pain score was 8/10 (interquartile range, 6, 8). After 12 weeks, we measured no statistically significant difference between groups in the primary outcome, intercourse pain score, or any secondary outcome measure. For both groups together, the median intercourse pain score diminished by 50% after 4 weeks and 75% after 12 weeks (P < 0.001). The most tender anatomic area, the vulvar vestibule, improved by 82% to 100% (P < 0.001) with therapy. We did not measure a statistically significant difference in serum estradiol levels or endometrial stripe thickness between groups. Conclusion: Estradiol cream applied to the vulvar vestibule, paired with precoital silicone lubricant, is a promising alternative to vaginal therapy for dyspareunia.

### New Topical Therapy for Provoked Vestibulodynia: Improvement of Psychological and Sexual Well-Being

Francesco De Seta, Patrizia Ianniello, Stefania Carlucci, Luigi Nappi, Felice Sorrentino, Guglielmo Stabile Int J Environ Res Public Health. 2023 Jan 20;20(3):1931. doi: 10.3390/ijerph20031931. https://pubmed.ncbi.nlm.nih.gov/36767294/ Vulvodynia is a vulvar discomfort that occurs in the absence of any specific, clinically identifiable disorder. Few therapies have shown to be effective for the treatment of vulvodynia. In our recently published study, we tested a drug-free gel in women affected by vulvar vestibulitis. It is a cosmetic gel which acts locally without any metabolic, pharmacological or immunological effect. In order to further promote the validity of this new product, in this manuscript we analyzed the results obtained from the administration of four questionnaires in the same two groups of women affected by PVD and treated with a placebo and the new product. The questionnaires used: Female Sexual Function Index Scoring (FSFI), Female Sexual Distress Scale (FSDS), Hospital Anxiety and Depression Scale (HADS), and health-related quality of life measured by SF-36 (SF-36). The results obtained by this current analysis showed that the new gel has also proven benefits on women's quality of life and sexual function, including improvements in arousal, desire, orgasm and satisfaction.

#### Evaluation and Treatment of Vulvodynia: State of the Science

Judith M. Schlaeger CNM, PhD, LAc, Jennifer E. Glayzer BSN, RN, Michelle Villegas-Downs MS, RN, Hongjin Li PhD, RN, Edward J. Glayzer PhD, Ying He PhD, Miho Takayama PhD, RN, LAc, Hiroyoshi Yajima PhD, LAc, Nobuari Takakura PhD, LAc, William H. Kobak MD, Barbara L. McFarlin CNM, PhD First published: 19 December 2022

https://onlinelibrary.wiley.com/doi/10.1111/jmwh.13456

Vulvodynia affects 7% of American women, yet clinicians often lack awareness of its presentation. It is underdiagnosed and often misdiagnosed as vaginitis. The etiology of vulvodynia remains unknown, making it difficult to identify or develop effective treatment methods. The purpose of this article is to (1) review the presentation and evaluation of vulvodynia, (2) review the research on vulvodynia treatments, and (3) aid the clinician in the selection of vulvodynia treatment methods. The level of evidence to support vulvodynia treatment varies from case series to randomized controlled trials (RCTs). Oral designamine with 5% lidocaine cream, intravaginal diazepam tablets with intravaginal transcutaneous electric nerve stimulation (TENS), botulinum toxin type A 50 units, enoxaparin sodium subcutaneous injections, intravaginal TENS (as a single therapy), multimodal physical therapy, overnight 5% lidocaine ointment, and acupuncture had the highest level of evidence with at least one RCT or comparative effectiveness trial. Pre to post-test reduction in vulvar pain and/or dyspareunia in non-RCT studies included studies of gabapentin cream, amitriptyline cream, amitriptyline with baclofen cream, up to 6 weeks' oral itraconazole therapy, multimodal physical therapy, vaginal dilators, electromyography biofeedback, hypnotherapy, cognitive behavioral therapy, cold knife vestibulectomy, and laser therapy. There is a lack of rigorous RCTs with large sample sizes for the treatment of vulvodynia, rendering it difficult to determine efficacy of most treatment methods. Clinicians will be guided in the selection of best treatments for vulvodynia that have the highest level of evidence and are least invasive.

**Exploring the health care experiences of women diagnosed with vulvodynia** Lauren Templeman, Judith Eberhardt, Jonathan Ling J Sex Med. 2023 Jan 14;20(1):97-106. doi: 10.1093/jsxmed/qdac023. https://pubmed.ncbi.nlm.nih.gov/36897241/

**Background:** Although seeking diagnosis and treatment for chronic pain should be straightforward, this is not typically the case for those living with vulvodynia, who often describe it as a battle, frequently involving misdiagnosis, dismissal, and gender-based discrimination. **Aim:** This study explored the health

care experiences of women living with vulvodynia in the United Kingdom. Methods: As they are less explored in literature, experiences postdiagnosis and across varying health care settings were specifically considered. Interviews were conducted with 6 women aged 21 to 30 years to explore their experiences when seeking help for vulvodynia. Outcomes: Through interpretative phenomenological analysis, 5 themes emerged: the impact of diagnosis, patients' perception of health care, self-guidance and lack of direction, gender as a barrier to effective care, and a lack of consideration of psychological factors. Results: Women often experienced difficulties before and after diagnosis, and many felt that their pain was dismissed and ignored due to their gender. Pain management was felt to be prioritized by health care professionals over well-being and mental health. Clinical implications: There is a need for further exploration of gender-based discrimination experiences among patients with vulvodynia, health care professionals' perceptions of their capabilities in working with such patients, and the impact of improving professionals' training in working with these patients2. Strengths and limitations: Health care experiences after diagnosis are rarely examined within literature, with studies predominantly focusing on experiences surrounding diagnosis, intimate relationships, and specific interventions. The present study provides an in-depth exploration of health care experiences through participants' lived experiences and gives insight into an underresearched area. Women with negative experiences of health care may have been more likely to participate than those with positive experiences, which may have resulted in their overrepresentation. Furthermore, participants were predominantly young White heterosexual women, and almost all had comorbidities, further limiting generalizability. **Conclusion:** Findings should be used to inform health care professionals' education and training to improve outcomes for those seeking care for vulvodynia.

"Time is on my side". Disease trajectory of vulvodynia: a systematic review with a narrative synthesis G E Cetera, C E M Merli, F Facchin, G Barbara, C Caia, G Libutti, V Boero Arch Gynecol Obstet. 2023 Mar 4. doi: 10.1007/s00404-023-06984-z. https://pubmed.ncbi.nlm.nih.gov/36869940/

Purpose: The aim of this systematic review was to shed light on the disease-trajectory of vulvodynia and identify potential risk factors which may affect such trajectory. Methods: We searched Pubmed to identify articles providing evidence on vulvodynia trajectory (i.e., remission, relapse or persistence rates) with a minimum follow-up of 2 years. A narrative approach was used for data synthesis. Results: Four articles were included (total participants: 741 women with vulvodynia; 634 controls). At a 2-year followup, 50.6% of women reported remission, remission with relapse was observed in 39.7% and persistence throughout time occurred in 9.6%. A decrease in pain was observed in 71.1% of patients at a 7-year follow-up. Mean pain scores and depressive symptoms resulted lower at 2-year follow-up, whereas sexual function and satisfaction were increased. Factors associated with remission of vulvodynia were greater couple cohesion, decreased reporting of pain after intercourse and lower levels of worst pain. Risk factors for symptom persistence included marriage, more severe pain ratings, depression, pain with partner touch, interstitial cystitis, pain with oral sex, fibromyalgia, older age and anxiety. Recurrence was associated with: longer duration of pain, more severe ratings of the worst pain ever and pain described as provoked. Conclusions: Symptoms of vulvodynia seem to improve over time, regardless of treatment. This finding contains a key message for patients and their physicians, considering the deleterious consequences of vulvodynia on women's lives.

### Are virtual consultations suitable for patients with vulval disease? A multicentre audit of outcomes in the COVID-19 pandemic

Fiona M Lewis, Sheila M McSweeney, Jeanne Wendling, Micheline Moyal-Barracco Skin Health Dis. 2022 Oct 10;3(1):e178. doi: 10.1002/ski2.178. eCollection 2023 Feb. https://pubmed.ncbi.nlm.nih.gov/36751328/

Background: During the COVID-19 pandemic, virtual consultation (VC) was used to replace in-person consultations. This raises specific questions when dealing with vulval conditions. Objectives: To assess the feasibility and the efficiency of VC with and without supplementary imaging, in patients with vulval conditions, and to evaluate the images provided as an aid to diagnosis. Methods: This prospective multicentre audit took place in three specialized vulval clinics in London and Paris. Anonymized data on patients' clinical characteristics, consultation characteristics (including the number and quality of any supplementary images provided) and consultation outcomes (diagnostic certainty and physician satisfaction) were collected. Characteristics and outcomes in those with or without supplementary imaging were compared amongst both new and follow-up consultations. Results: A total of 316 VCs were included. In total, 18.7% (n = 59) were new patient consultations and 81.3% (n = 257) were followup. Supplementary imaging (photographs and/or video recordings) were provided by 28.5% (n = 90) of the total cohort. Median photographic quality was significantly higher on a five-point Likert-type scale when photographs were taken by a third party as opposed to the patient themselves (4 vs. 3, Mann-Whitney U-test, p < 0.0001). There was no association between the provision of supplementary imaging and diagnostic certainty amongst new patient consultations. However, a higher proportion of follow-up patients who provided supplementary imaging received definitive management decisions ( $\chi^2$  test, p < 10.001) and physician satisfaction with these consultations, as measured on a five-point Likert-type scale, was significantly higher (Mann-Whitney U-test, p < 0.0001). Furthermore, median physician satisfaction scores ≥4 were observed in follow-up consultations for candidiasis, lichen simplex/eczema and vulvodynia. **Conclusions:** Although in-person consultation remains the gold standard of care, VC may have a role in the management of selected patients with vulval disease. It is possible to provide goodquality photographs for clinical assessment, particularly with the help of a third party and follow-up patients with an established, cancer-unrelated diagnosis may be best suited for this consultation modality.

# Women's Experience of Living with Vulvodynia Pain: Why They Participated in a Randomized Controlled Trial of Acupuncture

Allissa A Desloge, Crystal L Patil, Jennifer E Glayzer, Marie L Suarez, William H Kobak, Monya Meinel, Alana D Steffen, Larisa A Burke, Yingwei Yao, Miho Takayama, Hiroyoshi Yajima, Ted J Kaptchuk, Nobuari Takakura, David C Foster, Diana J Wilkie, Judith M Schlaeger J Integr Complement Med. 2023 Jan;29(1):50-54. doi: 10.1089/jicm.2022.0647. Epub 2022 Sep 21. https://pubmed.ncbi.nlm.nih.gov/36130137/

**Introduction:** Vulvodynia is vulvar pain lasting at least 3-months without clear identifiable cause that may have other associated factors. The aim, to explore motivations of women participating in a doubleblind randomized controlled trial of acupuncture for vulvodynia. **Methods:** Responses to the question: "Tell me about why you decided to participate in this study" were analyzed using conceptual content analysis to identify patterns in motivation for study participation. **Results:** Four patterns emerged: 1) desire to address uncontrolled pain, 2) desire for understanding, 3) wish to contribute to knowledge generation, and 4) need to remove cost barriers. **Conclusion:** Motivations indicate vulvodynia-specific aspects of acceptability of acupuncture. **Clinical Trial Registration:** <u>NCT03364127</u>.

#### Chronic Vulvar Pain and Health-Related Quality of Life in Women with Vulvodynia

Gabriela Patla, Agnieszka I Mazur-Bialy, Magdalena Humaj-Grysztar, Joanna Bonior Life (Basel). 2023 Jan 24;13(2):328. doi: 10.3390/life13020328. https://pubmed.ncbi.nlm.nih.gov/36836685/

The aim of this study was to investigate the severity of chronic vulvar pain in women with vulvodynia and its impact on their health-related quality of life (QL). The study group consisted of 76 women aged 19 to 58. The study was carried out using the diagnostic survey method, i.e., (1) the questionnaire technique, comprising (A) the author's questionnaire (76 questions) and (B) the WHOQOL-BREF questionnaire, and (2) the VAS. When analyzing the severity of vulvar pain on the VAS, the highest proportion of women rated it at level 6 (23.68%). This was significantly determined by certain personal characteristics (age < 25 years old) and sociodemographic characteristics (marital status: unmarried women, divorcees, widows; high school education), each at p < 0.05. Vulvodynia causes a significant deterioration (64.47%) in QL, which is mainly caused by a reduction in the ability to perform activities of daily living (27.63%) and a decrease in sexual satisfaction (27.63%). The level of stress significantly exacerbates pain (p < 0.05). The severity correlates significantly (p < 0.05) and negatively (r < 0) with QL perception, which was rated worst in the physical domain. The use of treatment resulted in a significant improvement in the physical and psychological domains (p < 0.05), and the latter was particularly influenced by physiotherapy (p < 0.05).

"It's all my fault": a qualitative study of how heterosexual couples experience living with vulvodynia Linn Myrtveit-Stensrud, Gro Killi Haugstad, Silje Endresen Rème, Sidsel Louise Schaller, Karen Synne Groven

Acta Obstet Gynecol Scand. 2023 Mar 6. doi: 10.1111/aogs.14537. https://pubmed.ncbi.nlm.nih.gov/36879489/

**Introduction:** Vulvodynia, a chronic genital pain disorder with a high lifetime prevalence among women, has a significant negative impact on both women and their partners. Although there is a growing body of literature on the experiences of women with vulvodynia, there has been little research on the condition's implications for partners and romantic relationships. The aim of this study is to explore how heterosexual couples experience living with vulvodynia. Material and methods: Eight Norwegian women diagnosed with vulvodynia by gynecologists were recruited with their partners (couples aged 19-32 years). Data was collected via individual semi-structured interviews and analyzed using inductive thematic analysis. **Results:** Three main themes were identified in the analysis: Mysterious disorder, Social exclusion and Sexual expectations. The results show that the couples struggle with understanding the pain, as well as navigating their social and sexual lives. We discuss these findings in light of a new theoretical model: the fear-avoidance-endurance model of vulvodynia. Conclusions: Heterosexual couples living with vulvodynia experience communication difficulties with partners, health professionals, and their social network. This sustains avoidance and endurance behavior, increasing pain and dysfunction over time and giving rise to feelings of powerlessness and loneliness. Social expectations regarding male and female sexuality also promote guilt and shame for both parties in couples affected by vulvodynia. Our results suggest that heterosexual couples living with vulvodynia, as well as health professionals treating them, should be helped to communicate more effectively in order to break vicious circles of maladaptive avoidance and endurance behavior.

#### Chronic Pelvic Pain

Pelvic mapping to explore patterns of chronic pelvic pain Kelli Aibel, Sharon Choi, Robert Moldwin Neurourol Urodyn. 2023 Feb 25. doi: 10.1002/nau.25145. https://pubmed.ncbi.nlm.nih.gov/36840909/

Purpose: Chronic pelvic pain syndromes (CPPS) are commonly encountered by urologists and urogynecologists and pose diagnostic and therapeutic challenges. Body maps have been helpful adjuncts to verbal descriptions of pain and may serve a role in phenotyping what is known to be a heterogeneous patient population. The aim of this study was to assess whether patterns of pain as marked on a body map of the pelvis exist among common CPPS diagnoses. The secondary aim was to investigate the association between the total number of pain locations marked on the map and clinical indices in patients with 1 to 3 CPPS diagnoses. Materials and methods: Data was collected on patients who visited the Northwell Health Pelvic Pain Treatment Center (PPTC) from January to May 2022 and were diagnosed with at least one of four major CPPS diagnoses: interstitial cystitis/bladder pain syndrome (IC/BPS), pelvic floor myalgia (PFM), chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), and vulvodynia. Demographic data as well as survey data from pelvic pain maps, Genitourinary Pain Index (GUPI) forms, and the short form-6 of the Pain Catastrophizing Scale (PCS-6) were recorded. Descriptive statistics among CPPS groups and Pearson correlations among the number of CPPS diagnoses were computed. **Results:** One hundred seventy females and 125 males with CPPS were included in the study. Significant cross-over in mapping patterns was notable between IC/BPS and PFM groups, both most commonly marking "abdomen" and "genital" regions. The most distinct pattern of pain was seen in patients with CP/CPPS and in patients with vulvodynia. Among the total sample, as the mean number of pain locations marked within the pelvis increased, GUPI and PCS scores increased (p < 0.05). As the number of CPPS diagnoses increased, the strength of the relationship independently increased. **Conclusions:** Pelvic body mapping demonstrated that different forms of CPPS displayed different distributions of pain, but mapping was not predictive of any diagnostic group. Nevertheless, the pelvic body map proved useful in identifying precise locations of pain and may help uncover regions of pain that cannot be easily communicated. The total number of pain sites marked appeared to correlate with worse clinical features.

#### Pelvic Pain in Transgender People Using Testosterone Therapy

Sav Zwickl, Laura Burchill, Alex Fang Qi Wong, Shalem Y Leemaqz, Teddy Cook, Lachlan M Angus, Kalen Eshin, Charlotte V Elder, Sonia R Grover, Jeffrey D Zajac, Ada S Cheung LGBT Health. 2023 Jan 4. doi: 10.1089/Igbt.2022.0187. https://pubmed.ncbi.nlm.nih.gov/36603056/

**Purpose:** This descriptive study aimed to assess the characteristics of pelvic pain and explore predictive factors for pelvic pain in transgender (trans) individuals using testosterone therapy. **Methods:** An online cross-sectional survey was open between August 28, 2020, and December 31, 2020, to trans people presumed female at birth, using testosterone for gender affirmation, living in Australia, and >16 years of age. The survey explored characteristics of pelvic pain following initiation of testosterone therapy, type and length of testosterone therapy, menstruation history, and relevant sexual, gynecological, and mental health experiences. Logistic regression was applied to estimate the effect size of possible factors contributing to pain after starting testosterone. **Results:** Among 486 participants (median age = 27

years), 351 (72.42%) reported experiencing pelvic pain following initiation of testosterone therapy, described most commonly as in the suprapubic region and as "cramping." Median duration of testosterone therapy was 32 months. Persistent menstruation, current or previous history of post-traumatic stress disorder, and experiences of pain with orgasm were associated with higher odds of pelvic pain after testosterone therapy. No association was observed with genital dryness, intrauterine device use, previous pregnancy, penetrative sexual activities, touching external genitalia, or known diagnoses of endometriosis, vulvodynia, vaginismus, depression, anxiety, or obesity. **Conclusions:** Pelvic pain is frequently reported in trans people following initiation of testosterone therapy. Given the association with persistent menstruation and orgasm, as well as the known androgen sensitivity of the pelvic floor musculature, further research into pelvic floor muscle dysfunction as a contributor is warranted.

### Clinical Approach to Recurrent Voiding Dysfunction, Dysuria, and Pelvic Pain Persisting for at Least 3 Months

Su Jin Kim, Khae Hawn Kim Int Neurourol J. 2022 Sep;26(3):179-189. doi: 10.5213/inj.2244200.100. Epub 2022 Sep 30. https://pubmed.ncbi.nlm.nih.gov/36203251/

There are several patients with urination problems and urethral and pelvic discomfort. Usually, these patients' symptoms are persistent and ambiguous; therefore, it is difficult to find underlying diseases associated with the patient's symptoms. In addition, there are various conditions such as overactive bladder, cystitis, and interstitial cystitis/bladder pain syndrome (IC/BPS). Sometimes patients with other chronic disorders such as fibromyalgia, inflammatory bowel syndrome, and vulvodynia show urination problems and pelvic pain. Thus, a patient-centered approach is important to find the cause of chronic urination problems and pelvic pain. Moreover, IC/BPS should be considered during the diagnostic process because the clinical characteristics of IC/BPS are diverse. In this narrative review, we suggest an integral approach for the diagnosis and treatment of IC/ BPS.

# Is Erbium/Neodymium Laser Combination Therapy an Effective Treatment Option for Interstitial Cystitis/Bladder Pain Syndrome With Vulvodynia?

Nobuo Okui, Machiko Okui, Marco Gambacciani Cureus. 2022 Nov 8;14(11):e31228. doi: 10.7759/cureus.31228. eCollection 2022 Nov. https://pubmed.ncbi.nlm.nih.gov/36505169/

Interstitial cystitis/bladder pain syndrome (IC/BPS) is often associated with vulvodynia and poor vaginal health. IC/BPS causes pelvic and bladder pain and urinary symptoms, which considerably reduce the quality of life. To date, this condition has no definitive cure. Local estrogen therapy (LET) has been proposed as a treatment for vulvodynia and poor vaginal health to improve the symptoms of IC/BPS. However, chronic LET could be contraindicated or not desired in some patients. The present study reports the case of a 55-year-old postmenopausal woman with IC/BPS who was successfully treated with combined vaginal erbium (VEL)/neodymium (Nd:YAG) laser (VEL+Nd:YAG) therapy. The patient presented with a five-year history of pelvic pain and urinary frequency. Direct approaches for the bladder (such as hydrodistension, anticholinergic drugs, and transurethral Hunner lesion ablation/cauterization) were conducted with inconsistent results. Immediately prior to the patient's presentation, LET was administered for 12 weeks; however, this therapy resulted in mild improvement and poor patient satisfaction. After presentation, VEL+Nd:YAG therapy was conducted once a month for

three months. The patient reported considerable decrease in pain during urination. The improved symptoms were maintained for six months after the last therapy session. These results suggest that VEL+Nd:YAG therapy is an effective method for improving symptoms in patients with IC/BPS

#### Persistent Genital Arousal Disorder

# Lumbar endoscopic spine surgery for persistent genital arousal disorder/genitopelvic dysesthesia resulting from lumbosacral annular tear-induced sacral radiculopathy

Choll W Kim, Irwin Goldstein, Barry R Komisaruk, Sue W Goldstein, Noel N Kim, Rose Hartzell-Cushanick, Maria Uloko, Alyssa Yee J Sex Med. 2023 Feb 14;20(2):210-223. doi: 10.1093/jsxmed/qdac017.

https://pubmed.ncbi.nlm.nih.gov/36763933/

Background: Persistent genital arousal disorder/genitopelvic dysesthesia (PGAD/GPD) is characterized by distressing, abnormal genitopelvic sensations, especially unwanted arousal. In a subgroup of patients with PGAD/GPD, cauda equina Tarlov cyst-induced sacral radiculopathy has been reported to trigger the disorder. In our evaluation of lumbosacral magnetic resonance images in patients with PGAD/GPD and suspected sacral radiculopathy, some had no Tarlov cysts but showed lumbosacral disc annular tear pathology. Aim: The aims were 2-fold: (1) to utilize a novel multidisciplinary step-care management algorithm designed to identify a subgroup of patients with PGAD/GPD and lumbosacral annular tearinduced sacral radiculopathy who could benefit from lumbar endoscopic spine surgery (LESS) and (2) to evaluate long-term safety and efficacy of LESS. Methods: Clinical data were collected on patients with PGAD/GPD who underwent LESS between 2016 and 2020 with at least 1-year follow-up. LESS was indicated because all had lumbosacral annular tear-induced sacral radiculopathy confirmed by our multidisciplinary management algorithm that included the following: step A, a detailed psychosocial and medical history; step B, noninvasive assessments for sacral radiculopathy; step C, targeted diagnostic transforaminal epidural spinal injections resulting in a temporary, clinically significant reduction of PGAD/GPD symptoms; and step D, surgical intervention with LESS and postoperative follow-up. Outcomes: Treatment outcome was based on the validated Patient Global Impression of Improvement, measured at postoperative intervals. Results: Our cohort included 15 cisgendered women and 5 cisgendered men (mean  $\pm$  SD age, 40.3  $\pm$  16.8 years) with PGAD/GPD who fulfilled the criteria of lumbosacral annular tear-induced sacral radiculopathy based on our multidisciplinary management algorithm. Patients were followed for an average of 20 months (range, 12-37) post-LESS. Lumbosacral annular tear pathology was identified at multiple levels, the most common being L4-L5 and L5-S1. Twenty-two LESS procedures were performed in 20 patients. Overall, 80% (16/20) reported improvement on the Patient Global Impression of Improvement; 65% (13/20) reported improvement as much better or very much better. All patients were discharged the same day. There were no surgical complications. Clinical implications: Among the many recognized triggers for PGAD/GPD, this subgroup exhibited lumbosacral annular tear-induced sacral radiculopathy and experienced long-term alleviation of symptoms by LESS. Strengths and limitations: Strengths include long-term post-surgical follow-up and demonstration that LESS effectively treats patients with PGAD/GPD who have lumbosacral annular tear-induced sacral radiculopathy, as established by a multidisciplinary step-care management algorithm. Limitations include the small study cohort and the unavailability of a clinical measure specific for PGAD/GPD. **Conclusion:** LESS is safe and effective in treating patients with PGAD/GPD who are diagnosed with lumbosacral annular tear-induced sacral radiculopathy.

### **Persistent Genital Arousal Disorder: Two Case Studies and Exploration of a Novel Treatment Modality** Meghan Scantlebury, Romeo Lucas

Womens Health Rep (New Rochelle). 2023 Feb 14;4(1):84-88. doi: 10.1089/whr.2022.0097. eCollection 2023.

https://pubmed.ncbi.nlm.nih.gov/36874234/

Persistent genital arousal disorder (PGAD) is characterized by persistent unwanted feelings of sexual arousal that can be debilitating. Despite first being defined >20 years ago, the precise etiology and treatment of this disorder remain elusive. Mechanical disruption of nerves, neurotransmitter changes, and cyst formation have all been considered as etiologies involved with the development of PGAD. With limited and ineffective treatment modalities, many women live with their symptoms untreated or undertreated. To broaden the literature, we present two cases of PGAD and present a novel treatment modality of the disorder with the use of a pessary. Although there was subjective success in dampening the symptoms, they were not completely resolved. These findings open the door for the potential of similar treatments in the future.

# Examining the Psychometric Properties of the HBI-19 Scale in a Sample of Women with Persistent Genital Arousal Symptoms

M E Mulroy, R A Jackowich, C F Pukall J Sex Res. 2023 Feb 24;1-11. doi: 10.1080/00224499.2023.2176423. https://pubmed.ncbi.nlm.nih.gov/36826430/

Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD) is a highly distressing, yet poorly understood health concern characterized by persistent, unwanted, and unpleasant genital arousal sensations in the absence of psychological arousal and desire. PGAD/GPD symptoms can be reduced by engaging in frequent sexual behaviors, meaning that hypersexual behavior may be present as a feature of PGAD/GPD in some cases. Given this association and the current lack of measures designed for assessment of PGAD/GPD specifically, the present study aimed to investigate the psychometric properties of the Hypersexual Behavior Inventory (HBI-19) in a sample of women with PGAD/GPD symptoms. Specifically, the factor structure of the HBI-19 was explored via Exploratory Factor Analysis (EFA) as well as evaluation of model fit indices and reliability indices (Cronbach's alpha). EFA revealed a two-factor structure for the HBI-19 in the sample of women with PGAD/GPD symptoms, differing from the originally validated three-factor structure. RMSEA as well as TLI values suggested poor fit for all three models examined, including the two-factor model, while SRMR suggested good fit for the two-factor and three-factor model and suggested poor fit for the one-factor models. These findings suggest measurement non-invariance at the configural level and indicate that hypersexual behavior is best understood as a possible feature of PGAD/GPD as opposed to a core element of PGAD/GPD.

### Pudendal Neuralgia

Clinical usefulness of quantitative thermal sensory testing in the diagnosis and surgical treatment of women with pudendal neuropathy

Jacques Beco, Laurence Seidel, Adelin Albert Neurol Sci. 2023 Feb 14. doi: 10.1007/s10072-023-06663-6. https://pubmed.ncbi.nlm.nih.gov/36781566/ Background: The aim of this study, conducted on women with pudendal neuropathy, was to evaluate the usefulness of quantitative thermal sensory testing (QTST) in the diagnosis, surgical management, and prognosis of the disease. Methods: The study was conducted on 90 women with pudendal neuropathy. QTST in pudendal nerve sensory innervation territory was realized before and more than 24 months after operative pudendoscopy on most patients. Cold and warm thresholds were evaluated together with a search for qualitative anomalies. The diagnostic value of QTST was assessed by comparing baseline data with normative values previously derived from 41 presumably healthy women. The effect of operative pudendoscopy on thermal sensitivity was tested by comparing preoperative and postoperative measurements. Assessment of the long-term prognostic value of QTST was based on "surgical success" defined as a VAS pain level less than 4 at least 2 years after surgery. Results: The existence of qualitative anomalies, like anesthesia, allodynia, dysesthesia, radiation, and dyslocalization, was clearly indicative of pudendal neuropathy. The presence of after sensation and "out of limit" values of skin temperature and cold detection threshold were also helpful for diagnosing the disease. Surgery reduced qualitative anomalies but had no positive effect on QTST thresholds. QTST measurements had no real prognostic value but other factors like constipation and abnormal perineal descent were predictive of surgical success. **Conclusion:** For women with pudendal neuropathy, QTST can be considered a useful, non-invasive tool in the diagnosis, and management of the disease, but it cannot predict satisfactorily long-term outcome of operative pudendoscopy.

Dorsal Root Ganglion Stimulation Therapy for Refractory Idiopathic Pudendal Neuralgia Gaurav Chauhan, Suresh K Srinivasan, Suchit Khanduja Cureus. 2023 Feb 6;15(2):e34681. doi: 10.7759/cureus.34681. eCollection 2023 Feb. https://pubmed.ncbi.nlm.nih.gov/36909041/

Dorsal root ganglion stimulation is a relatively new treatment option for chronic pain conditions such as pudendal neuralgia, which is a chronic pain condition affecting the pudendal nerve in the pelvic region. Pudendal neuralgia is a debilitating condition that can significantly affect the patient's quality of life. In dorsal root ganglion stimulation, a small device is implanted that delivers electrical impulses to the dorsal root ganglion to modulate pain signals coming from the pudendal nerve. The procedure is considered investigational and has been investigated in case series and case reports with promising results. However, more research is needed to fully understand its safety and effectiveness. This case report highlights the potential of dorsal root ganglion stimulation as a treatment option for pudendal neuralgia and the need for further research to establish it as a standard treatment option.

### Could Horse Gait and Induced Pelvic Dynamic Loads in Female Equestrians Be a Risk Factor in Pudendal Neuralgia?

Sébastien Murer, Guillaume Polidori, Fabien Beaumont, Fabien Bogard, Hassen Hakim, Fabien Legrand Sports (Basel). 2023 Jan 10;11(1):16. doi: 10.3390/sports11010016. https://pubmed.ncbi.nlm.nih.gov/36668720/

Pudendal Neuralgia (PN) is a rare, debilitating disease caused by damage to the pudendal nerve, which innervates the anus, rectum, perineum, lower urinary tract, and genitalia. Although its etiology remains scientifically unknown, a number of sports practices, including horse-riding, are reported as triggering and/or aggravating factors. The present work summarizes the experimental measurements of the contact pressure at the interface between the rider and saddle, for a population of 12 experienced

female riders. These tests reveal that dynamic horseback-riding leads to high levels of peak pressures in the perineal region, which confirms that the practice of equine sports may cause neuropathologies such as PN. All collected data will be used as boundary conditions in a future numerical 3D model aimed at locating the possible areas of pudendal nerve crushing.

**Comments on "Sacral Nerve Stimulation in Patients With Refractory Pudendal Neuralgia"** Simone Vigneri, Marco La Grua, Gianfranco Sindaco, Matteo Zanella Pain Physician. 2022 Sep;25(6):E884-E885. https://www.painphysicianjournal.com/current/pdf?article=NzU0NQ%3D%3D&journal=146

To the Editor: We read with great interest the article entitled "Sacral Nerve Stimulation in Patients With Refractory Pudendal Neuralgia" by Kai-Kai et al (1) recently published in the July 2022 issue. We commend the authors for addressing the effectiveness of neuromodulation in a disorder with high burden such as pudendal neuralgia. In a population of 56 eligible patients, 33 patients with pudendal neuralgia were treated with sacral nerve stimulation (SNS) and the authors concluded that the treatment improved pain severity and sleep time either in short- and long-term (up to 6 months) with significant reduction of analgesic intake. However, there are several aspects of this study that need to be clarified.

#### **Pudendal Nerve Block**

Shirin Ghanavatian, Stephen W. Leslie, Armen Derian In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. 2022 Nov 28. https://www.ncbi.nlm.nih.gov/books/NBK551518/

Pudendal nerve blocks are the method of choice utilized for the initial diagnosis and management of chronic pelvic pain caused by pudendal neuralgia, commonly due to pudendal nerve entrapment. Additionally, a pudendal nerve block is a widely used regional anesthesia technique performed for gynecologic, obstetrical, and anorectal procedures.

#### **Pudendal Nerve Entrapment Syndrome**

Jasmeen Kaur, Stephen W. Leslie, Paramvir Singh In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. 2022 Nov 28. https://pubmed.ncbi.nlm.nih.gov/31334992/

Pudendal neuralgia caused by pudendal nerve entrapment (PNE) is a chronic and often severely disabling neuropathic pain syndrome. It presents in the sensory distribution region of the pudendal nerve and affects both males and females. The most characteristic symptom, found in over 50% of patients, is perineal pain exacerbated by sitting, which is relieved by standing or lying. It is frequently misdiagnosed or underdiagnosed and inappropriately treated, initially causing a significant delay in proper management and severely negatively impacting the quality of life.

#### Anatomy of the Pudendal Nerve

The pudendal nerve emerges from the S2, S3, and S4 roots' ventral rami of the sacral plexus. It carries sensory, motor, and autonomic fibers; however, an injury to the pudendal nerve causes more sensory

effects than motor. It initially courses between two muscles, the piriformis and coccygeus muscles, then departs the pelvic cavity through the greater sciatic foramen ventral to the sacrotuberous ligament. It passes medial to and under the sacrospinous ligament at the level of the ischial spine to re-enter the pelvic cavity through the greater sciatic foramen. The pudendal nerve then courses in the pudendal canal, also called the Alcock canal. The three last branches of the pudendal nerve terminate in the ischioanal fossa. These are the inferior rectal branch, perineal branch, and dorsal sensory nerve of the penis or clitoris. However, there are case reports which have shown variability in the anatomy of the pudendal nerve. (See our companion article on Anatomy, Abdomen and Pelvis, Pudendal Nerve)

### Pudendal Nerve Compression Based on Anatomy

The pudendal nerve entrapment syndromes are subdivided into four types based on the location of the compression.

- Type I Entrapment below the piriformis muscle as the pudendal nerve exits the greater sciatic notch.
- Type II Entrapment between sacrospinous and sacrotuberous ligaments is the most common site of pudendal nerve entrapment.
- Type III Entrapment in the Alcock canal.
- Type IV Entrapment of terminal branches.

### **Dermatological Conditions**

# Comparison of electrophysiology therapy and glucocorticoid therapy in the treatment of 2 subtypes of vulvar epithelial non-neoplastic lesions: a prospective cohort study

Dongmei Wei, Jijie Li, Yueting Zhang, Jian Meng, Yueyue Chen, Xiaoyu Niu Ann Transl Med. 2023 Feb 28;11(4):175. doi: 10.21037/atm-23-224. https://pubmed.ncbi.nlm.nih.gov/36923075/

Background: Lichen-like lesions with degeneration and pigmentation alterations can be divided into the following 2 types: (I) chronic simple lichen; and (II) sclerosing lichen. The etiology of the disease is unknown. This study sought to examine the therapeutic effects of electrophysiological smooth-muscle electrical stimulation in the treatment of lichen-like lesions of the vulva. Methods: A total of 80 outpatients, who had been confirmed to have vulvar lichen-like lesions by vulvar biopsy at our hospital from November 2016 to March 2018, were prospectively included in this study. The patients received electrophysiology or glucocorticoid therapy. After completing a treatment cycle according to the clinical treatment routine, the outpatients were monitored at 1-, 3- and 6-month intervals. Patients used an improvement scale (i.e., the patient global impression of change scale) to score their subjective perceptions and subjective symptoms. The clinical curative effect scale was used to calculate the curative effect index and grade the curative effect. Results: After 1 month of treatment, the active enhancement of simple lichen in the electrophysiological treatment group and glucocorticoid treatment group improved, while the active enhancement of simple lichen in the electrophysiological treatment group improved after 3 months of treatment. After 6 months of treatment, the subjective improvement score of the electrophysiological treatment group was better than that of lichen sclerosus. After 3 months of treatment, the effective rate of the electrophysiological therapy group was better than that of the glucocorticoid therapy group. After 6 months of treatment in the electrophysiological treatment group, the efficacy of simple lichen is also better than that of sclerotic lichen. Conclusions: Conventional hormone therapy is easier for patients to accept because of its convenience and low costs.

#### Mid-term symptomatic relief after platelet-rich plasma infiltration in vulvar lichen sclerosus

Carola Medina Garrido, Alejandra Cano García, Lidia de la Cruz Cea, Ana B Oreja Cuesta Arch Dermatol Res. 2023 Jan 19. doi: 10.1007/s00403-023-02529-1. https://pubmed.ncbi.nlm.nih.gov/36656384/

**Purpose:** Vulvar lichen sclerosus (LS) is a chronic, progressive, autoimmune dermatologic condition that causes cutaneous changes accompanied by pruritus and pain. There remains a small population with vulvar LS refractory to topical corticosteroids. Injection of platelet-rich plasma (PRP) has been reported to have positive effects on tissue repair. The aim of this pilot study was to evaluate changes in symptom scores during and after PRP vulvar infiltration. **Methods:** Three PRP infiltrations were administered to 28 female postmenopausal patients with biopsy-proved LS with unsatisfactory response to steroid therapy. Change in score according to the Clinical Scoring System for Vulvar Lichen Sclerosus (CSS) was measured on six occasions over the course of a year. We used growth curve modeling to measure change over the period of the study. **Results:** Women in our study experienced a statistically significant improvement in auto-assessed symptoms of vulvar lichen sclerosus, and this improvement appears to be maintained throughout the monitoring year. **Conclusion:** Platelet-rich plasma may have a role in symptom relief in certain cases of patients with LS that do not respond to first-line therapy.

### Comparison of the efficacy of focused ultrasound at different focal depths in treating vulvar lichen sclerosus

Ru Jia, Can Wu, Xiaoxu Tang, Miaomiao He, Xinglin Liu, Chang Su, Chengzhi Li Int J Hyperthermia. 2023;40(1):2172220. doi: 10.1080/02656736.2023.2172220. https://pubmed.ncbi.nlm.nih.gov/36710083/

**Objective:** This study aimed to compare the efficacy and safety of focused ultrasound (FU) at different focal depths in treating vulvar lichen sclerosus (VLS). **Methods:** A retrospective study was conducted on 84 patients with VLS. Among them, 43 cases were treated with FU at a focal depth of 2.5 mm and 41 cases at a focal depth of 4.0 mm. Therapeutic time, treatment energy, postoperative efficacy, complications and recurrence rates were compared. **Results:** No statistically substantially differences in age, disease course, history of immune system diseases, lesion size and severity of symptoms were found between the two groups. All patients successfully received FU therapy. No significant difference in curative rate was observed between the two groups at 3, 6 and 12 months after FU therapy. At 12 months after FU therapy, the recurrence rate of the experimental group (FU treatment at 2.5 mm focal depth) was lower than the control group (FU treatment at 4.0 mm focal depth) (7.0% vs 24.4%, *p* = 0.027). The experimental group was treated for a shorter period of time [22.69 ± 0.64 (min) vs 24.93 ± 0.72(min), *p* = 0.022] and at a lower dose[5,026.05 ± 148.00(J) vs 5,484.26 ± 160.60(J) *p* = 0.039]. **Conclusion:** Compared with that at the routine focal depth (4.0 mm), FU therapy at a low treatment depth (2.5 mm) can achieve a similar therapeutic effect but lower recurrence rate, therapeutic time and treatment energy. This work provides insight into the optimization of clinical protocols.

**High-frequency ultrasound assessment of vulvar lichen sclerosus treated with photodynamic therapy** Yukun Wang, Jianchun Hao, Jie Liu

Photodiagnosis Photodyn Ther. 2023 Jan 5;41:103277. doi: 10.1016/j.pdpdt.2023.103277. https://pubmed.ncbi.nlm.nih.gov/36621633/ Background: Patients with vulvar lichen sclerosus (VLS) are faced with a decreased quality of life and an increased risk of vulvar malignancy. 5-Aminolevulinic acid-based photodynamic therapy (ALA-PDT) can serve as an alternative for refractory VLS patients. However, high-frequency ultrasound (HFUS) has never been introduced in the ALA-PDT outcome assessment for VLS patients. Methods: A prospective study was conducted. Refractory VLS patients received two treatment courses of ALA-PDT (3 times of remedies at 2-week intervals for each course), and underwent clinical, HFUS and histopathological assessment. Statistical analysis comparing parameters at baseline and after ALA-PDT was performed. Results: Thirty-one VLS patients were included. Both subjective symptoms (itch and burning pain) and objective severity (lesion size and hypopigmentation) were relieved significantly after ALA-PDT treatment. Hypoechoic dermal band (HDB) thickness revealed by HFUS decreased progressively with successive ALA-PDT treatment, and the reduction value had a positive correlation with the reduction of inflammatory infiltration depth in histopathology. Collagen homogenization depth decrease was also noticed. Besides, adverse effects were recorded, mainly as mild and transient post-treatment edema and pain. **Conclusions:** ALA-PDT is an effective and safe therapeutic option for refractory VLS patients. HFUS can act as a complement to the non-invasive treatment monitoring for its objectivity, quantifiability and precision in the distinct vertical perspective.

### A systematic review of laser therapy for vulvar skin conditions

Katherine Kim, Mansee Desai, Ashley Elsensohn, Christina N Kraus J Am Acad Dermatol. 2023 Jan 11;S0190-9622(23)00061-0. doi: 10.1016/j.jaad.2023.01.003. https://www.jaad.org/article/S0190-9622(23)00061-0/fulltext

*To the Editor:* While laser devices have been utilized for a variety of vulvar skin conditions, much of the literature focuses on laser use in vulvovaginal atrophy or genitourinary syndrome of menopause. Prior reviews have also shown limited evidence for clinical efficacy and safety of laser treatments in female gynecologic and urologic conditions. Herein, we conducted a systematic review of laser devices for neoplastic and inflammatory vulvar skin conditions. A literature search was conducted using PubMed, Ovid, and CINAHL using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines with search terms "vulvar" or "vulva" and "laser". Inclusion criteria consisted of articles published in English after 1990. Studies on rejuvenation and genitourinary syndrome of menopause were excluded. We identified 90 articles consisting of 2072 vulvar cases, comprising 23 diagnoses, treated by laser as monotherapy or in combination with other therapies (Supplementary Table I, available via Mendeley at <a href="https://doi.org/10.17632/f9sgx9nt2t.2">https://doi.org/10.17632/f9sgx9nt2t.2</a>).

# Elevated body mass index, statin use, and cholecystectomy are associated with vulvar lichen sclerosus: A retrospective, case-control study

Yen Luu, An-Lin Cheng, Colleen Reisz J Am Acad Dermatol. 2023 Feb 1;S0190-9622(23)00158-5. doi: 10.1016/j.jaad.2023.01.023. https://www.jaad.org/article/S0190-9622(23)00158-5/fulltext

*To the Editor*: Vulvar lichen sclerosus (VLS) is a chronic, progressive inflammatory dermatosis characterized by loss of vulvar architecture. Patients with VLS have a high risk of comorbid anxiety and depression; however, limited data exist on medical comorbidities among patients with VLS. Understanding comorbidities associated with VLS may provide perspectives for comprehensive

treatment of affected patients. Therefore, we examined comorbidities and medications among women with VLS from a single-site dermatology center (2019-2021) using a retrospective case-control study.

Lichen Sclerosus and Sexual Dysfunction: A Systematic Review and Meta-Analysis Rachel Pope, Min Ho Lee, Anna Myers, Junmin Song, Ramy Abou Ghayda, Jong Yeob Kim, Sung Hwi Hong, Se Bee Lee, Ai Koyanagi, Louis Jacob, Lee Smith, Jae II Shin https://pubmed.ncbi.nlm.nih.gov/36115787/

**Background:** Lichen sclerosus (LS) is a common autoimmune dermatological condition that is often under-diagnosed in women and has been documented to affect quality of life and sexual function. **Aim:** To determine the prevalence of sexual dysfunction among women with vulvar lichen sclerosus. Methods: The authors conducted a systematic review and meta-analysis of the existing research on LS and sexual function in database including PubMed using search terms: lichen sclerosus OR vulvar lichen sclerosus OR vulvar lichen sclerosus et atrophicus OR kraurosis vulvae) AND (sexual function OR sexual functions OR sexual disorder OR sexual disorders OR sexual activity OR sexual activities OR sexual dysfunction OR sexual dysfunctions OR dyspareunia OR vaginismus). Outcomes: Nearly 60% of women with lichen sclerosus suffer from sexual dysfunction. Results: Two hundred and ten studies were initially identified. Twenty-six articles met inclusion criteria and 3 were excluded as they did not relate to sexual function, were regarding a surgical or medical intervention and sexual dysfunction and one was a review article. Therefore, 23 studies were included in the final analysis resulting in a cumulative 486 participants with LS with 208 patients experiencing any kind of sexual dysfunction. Meta-analysis presented prevalence of sexual dysfunction among LS patients as 59% (95% CI: 48 - 70%). Dyspareunia or generalized pain with intercourse was the most commonly reported type of dysfunction. Clinical implications: Discussing sexual concerns with women with LS could empower them to seek treatment. Strengths and limitations: Few articles met criteria for inclusion. Conclusion: A large proportion of women with LS experience sexual dysfunction. More research is needed, especially that which includes biopsy-proven LS and validated tools on sexual function.

### Lichen sclerosus: The 2023 update

David A De Luca, Cristian Papara, Artem Vorobyev, Hernán Staiger, Katja Bieber, Diamant Thaçi, Ralf J Ludwig

Front Med (Lausanne). 2023 Feb 16;10:1106318. doi: 10.3389/fmed.2023.1106318. eCollection 2023. https://pubmed.ncbi.nlm.nih.gov/36873861/

Lichen sclerosus (LS) is an underdiagnosed inflammatory mucocutaneous condition affecting the anogenital areas. Postmenopausal women are predominantly affected and, to a lesser extent, men, prepubertal children, and adolescents. The etiology of LS is still unknown. Hormonal status, frequent trauma and autoimmune diseases are well-known associations for LS, yet infections do not seem to be clear risk factors. LS pathogenesis involves factors such as a genetic predisposition and an immune-mediated Th1-specific IFNy-induced phenotype. Furthermore, there is a distinct expression of tissue remodeling associated genes as well as microRNAs. Oxidative stress with lipid and DNA peroxidation provides an enabling microenvironment to autoimmunity and carcinogenesis. Circulating IgG autoantibodies against the extracellular matrix protein 1 and hemidesmosome may contribute to the progression of LS or simply represent an epiphenomenon. The typical clinical picture includes chronic whitish atrophic patches along with itching and soreness in the vulvar, perianal and penile regions. In addition to genital scarring, and sexual and urinary dysfunction, LS may also lead to squamous cell

carcinoma. Disseminated extragenital LS and oral LS are also reported. The diagnosis is usually clinical; however, a skin biopsy should be performed in case of an unclear clinical picture, treatment failure or suspicion of a neoplasm. The gold-standard therapy is the long-term application of ultrapotent or potent topical corticosteroids and, alternatively, topical calcineurin inhibitors such as pimecrolimus or tacrolimus. Collectively, LS is a common dermatological disease with a so far incompletely understood pathogenesis and only limited treatment options. To foster translational research in LS, we provide here an update on its clinical features, pathogenesis, diagnosis and (emerging) treatment options.