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Vulvodynia / Vulvovaginal Pain

Oral desipramine and topical lidocaine for vulvodynia: a randomized controlled trial.
Foster DC, Kotok MB, Huang LS, Watts A, Oakes D, Howard FM, Poleshuck EL, Stodgell CJ, Dworkin RH.
Obstet Gynecol. 2010 Sep;116(3):583-93.

OBJECTIVE: To estimate the efficacy of common treatments for vulvodynia: topical lidocaine monotherapy, oral desipramine monotherapy, and lidocaine-desipramine combined therapy. METHODS: A 12-week randomized, double-blinded, placebo-controlled trial was conducted on 133 vulvodynia-afflicted women assigned to four treatment arms: placebo tablets-placebo cream, desipramine tablets-placebo cream, placebo tablets-lidocaine cream, and desipramine tablets-lidocaine cream. The tampon test was selected as primary end point using a modified intention-to-treat analysis. Twelve secondary end points were also examined. At completion of the 12-week randomized phase, women were examined "open label" through 52 weeks postrandomization. RESULTS: All treatment arms reported substantial tampon-test pain reduction: 33% reduction placebo cream-placebo tablet, 20% reduction lidocaine cream-placebo tablet, 24% reduction placebo cream-desipramine tablet, and 36% reduction lidocaine cream-desipramine tablet. Compared with placebo, we found no significant difference in tampon-test pain reduction with desipramine (t=0.90; P=.37) or lidocaine (t=1.27; P=.21). Of the remaining 12 outcome measures, only the Index of Sexual Satisfaction, improved with desipramine compared with placebo (t=-2.81; P=.006). During the open-label phase, women undergoing vestibulectomy surgery reported significantly improved pain as measured by cotton swab test and the McGill Pain Scale compared with nonsurgical alternatives. CONCLUSION: Oral desipramine and topical lidocaine, as monotherapy or in combination, failed to reduce vulvodynia pain more than placebo. Placebo or placebo-independent effects are behind the substantial pain improvement seen in all treatment allocations.

Comfort in discussing vulvodynia.

Nguyen RHN, MacLehose R, Veasley C, Turner R, Harlow BL, Horvath K.

43rd Society for Epidemiologic Research Annual Meeting, Seattle, WA, June 23 – 26, 2010.

Social support may improve mental and physical health. To assess determinants of comfort in discussing vulvar pain with a spouse/partner, mother/sister, best friend, or other women friends among a sample of women with vulvodynia, we used data from 1,991 women with diagnosed vulvodynia who responded to a self-administered mailed questionnaire conducted by the National Vulvodynia Association. Comfort was assessed with a 4-point scale that was subsequently categorized into two (Never/Sometimes and Often/Always). Separate multivariable logistic regression models were fit for each of the four relationship types to estimate the association between comfort and characteristics of vulvar pain (time with pain, severity of recent pain, having a family member with pain). Independent of age, the longer women had vulvar pain, the less likely they were to speak about it in any type of relationship (adjusted odds ratio (OR) 0.96 for every year with vulvodynia, 95% confidence interval (CI) 0.93-0.98). Women were more comfortable discussing it with their mother/sister if they had a relative with vulvodynia (OR 2.29, 95% CI 1.2 – 4.3), and less comfortable if they were divorced (vs. married OR 0.57, 95% CI 0.35 – 0.91). Greater levels of comfort in discussing vulvar pain with best friends and other women friends was associated with a more severe level of vulvar pain in the last 6 months (best friends: OR 1.19, 95% CI 1.04 – 1.37; other women friends: OR 1.18, 95% CI 1.01 – 1.38). Our data suggest that characteristics of vulvar pain may determine how comfortable a woman feels in discussing her vulvodynia, and that these determinants are specific to the type of relationship. Relationship-specific campaigns to de-stigmatize discussions about vulvodynia could be developed.

Electrodiagnostic functional sensory evaluation of patients with generalized vulvodynia: a pilot study.

Murina F, Bianco V, Radici G, Felice R, Signaroldi M.

J Low Genit Tract Dis. 2010 Jul;14(3):221-4.

OBJECTIVE: To objectively evaluate vulvodynia by the current perception threshold (CPT) neurometer. METHODS: Neuroselective CPT measures of the pudendal nerve were obtained at the perineum by a neurometer (Neurotron, Inc, Baltimore, MD), using constant alternating sinusoid waveform electrical stimulus at 2,000-, 250-, and 5-Hz frequencies, in 20 healthy volunteers and 38 women with vulvodynia. The mean +/- SD CPT values in vulvodynia and healthy (control) women were analyzed with the Student t test. RESULTS: Women with vulvodynia showed lower mean CPT values ($p < .01$). CONCLUSIONS: Results of this study support a neuroselective sensory dysfunction in generalized vulvodynia. The field is opened for CPT measures in vulvodynia in selecting therapy strategy, monitoring response to treatment, and assessing vestibulodynia. Assessment of threshold values in a greater number of controls is needed to set a cutoff in CPT values for diagnosis and to grade the severity of the diseases.

Long-term results of an individualized, multifaceted, and multidisciplinary therapeutic approach to provoked vestibulodynia.
Spoelstra SK, Dijkstra JR, van Driel MF, Weijmar Schultz WC.
J Sex Med. 2010 Jul 14. [Epub ahead of print]

Introduction. Although it is highly recommended to use a multifaceted approach to treat provoked vestibulodynia (PVD), the large majority of treatment studies on PVD used a one-dimensional approach. Aim. To evaluate the long-term treatment outcome of a multifaceted approach to vulvar pain, sexual functioning, sexually related personal distress, and relational sexual satisfaction in women with PVD. Methods. Retrospective questionnaire survey 3-7 years after treatment. Main Outcome Measures. Sexual functioning, sexually related personal distress, and relational sexual satisfaction were measured using the Female Sexual Function Index (FSFI), the Female Sexual Distress Scale (FSDS), and the Dutch Relationship Questionnaire (NRV), respectively. An additional questionnaire assessed socio-demographic variables, intercourse resumption, and the level to which the women would recommend the treatment to other women with PVD. Post-treatment vulvar pain scores were obtained using a visual analog scale (VAS). Pretreatment scores were reported in retrospect on a separate VAS. Results. The questionnaires were completed by 64 out of 70 women (91%). Mean follow-up was 5 years (range 3-7). Comparison of the mean pretreatment and post-treatment VAS scores showed a significant reduction in vulvar pain. Pain reduction was reported by 52 women (81%), whereas no change and pain increase were reported by 7 women (11%) and 5 women (8%), respectively. Post-treatment, 80% of the women had resumed intercourse. Only 5 women (8%) reported completely pain-free intercourse. Comparisons with age-related FSFI and FSDS Dutch norm data showed that scores for sexual functioning in the study group were significantly lower, while scores for sexually related personal distress were significantly higher. There were no significant differences in relational sexual satisfaction ratings between the study group and the NRV Dutch norm data. Conclusion. These retrospective data on long-term treatment outcome support the hypothesis that a multifaceted approach to PVD can lead to substantial improvements in vulvar pain and the resumption of intercourse.

Parturition after vestibulectomy.
Burrows LJ, Sloane M, Davis G, Heller DS, Brooks J, Goldstein A.
J Sex Med. 2010 Aug 16. [Epub ahead of print]

ABSTRACT Introduction. Provoked vestibulodynia is the most common cause of sexual pain in premenopausal women. Vulvar vestibulectomy has been shown to be an effective treatment. Aim. To determine the optimum route of parturition in women who become pregnant after vulvar vestibulectomy. Methods. All women who underwent a complete vulvar vestibulectomy by one of four surgeons were contacted between 12 and 72 months after surgery. For all women who had a term pregnancy and subsequent delivery, the research assistant abstracted data from the charts. Descriptive statistics were applied. Main Outcome Measures. The number of women who underwent a delivery after a vestibulectomy, mode of delivery, and rate of perineal lacerations. Results. Of 109 women, 44 (40%) had undergone at least one term

pregnancy and delivery; 23 (52%) were vaginal, and 21 (48%) were cesarean deliveries. Of the vaginal deliveries, 11 (48%) were over an intact perineum. Three (13%) women had a midline episiotomy, none of which extended into third or fourth degree lacerations and one woman (4.4%) sustained a spontaneous fourth degree perineal laceration. Conclusions. Vaginal delivery after vulvar vestibulectomy appears to be a safe option, with no increased perineal morbidity above the general population. Furthermore, it is not an indication for a cesarean delivery.

Approach to the diagnosis and treatment of vulvar pain.
Danby CS, Margesson LJ.
Dermatol Ther. 2010 Sep;23(5):485-504.

Vulvar pain is a common problem, affecting up to 16% of women. The pain and discomfort seriously impacts their quality of life, and is compounded by the increasing frustration encountered in their search for appropriate medical advice. Their pain can be localized or generalized, constant or intermittent, with or without visible changes. For practitioners, the correct diagnosis and treatment of vulvar pain is a challenge. There is an extensive differential diagnosis, from problems that are simple and immediately visible to those that are much more complex and truly invisible. This review provides an approach to the diagnosis of vulvar pain. It outlines the wide range of etiologies for vulvar pain, and provides details of the most vexing in a comprehensive look at vulvodynia, including definition, theory, diagnosis, and therapy.

Chronic vulvar pain from a physical therapy perspective.
Hartmann D.
Dermatol Ther. 2010 Sep;23(5):505-513.

When assessing women with chronic vulvar pain, women's health physical therapists search for comorbid mechanical components (including musculoskeletal, fascial, and visceral) and other disorders that may contribute to or be caused by chronic vulvar pain (CVP). Pelvic floor hypertonicity is a key perpetuating factor for CVP. Comprehensive physical therapy evaluation and suggested physical therapy interventions are described. Anatomy of the pelvis, common evaluative findings, and specifics for pelvic floor muscle rehabilitation are presented. Normalization of pelvic floor muscle function contributes to the reduction of CVP. Successful treatment includes the identification and treatment of co-existing physical abnormalities throughout the trunk and pelvis.

Woman and partner-perceived partner responses predict pain and sexual satisfaction in provoked vestibulodynia couples.
Rosen NO, Bergeron S, Leclerc B, Lambert B, Steben M.
J Sex Med. 2010 Aug 4. [Epub ahead of print]

Introduction. Provoked vestibulodynia (PVD) is a highly prevalent vulvovaginal pain condition that results in significant sexual dysfunction, psychological distress, and reduced quality of life. Although some intra-individual psychological factors have been associated with PVD, studies to date have neglected the interpersonal context of this condition. Aim. We examined whether partner responses to women's pain experience-from the perspective of both the woman and her partner-are associated with pain intensity, sexual function, and sexual satisfaction. Methods. One hundred ninety-one couples (M age for women = 33.28, standard deviation [SD] = 12.07, M age for men = 35.79, SD = 12.44) in which the woman suffered from PVD completed the spouse response scale of the Multidimensional Pain Inventory, assessing perceptions of partners' responses to the pain. Women with PVD also completed measures of pain, sexual function, sexual satisfaction, depression, and dyadic adjustment. Main Outcome Measures. Dependent measures were women's responses to: (i) a horizontal analog scale assessing the intensity of their pain during intercourse; (ii) the Female Sexual Function Index; and (iii) the Global Measure of Sexual Satisfaction Scale. Results. Controlling for depression, higher solicitous partner responses were associated with higher levels of women's vulvovaginal pain intensity. This association was significant for partner-perceived responses (beta = 0.29, P < 0.001) and for woman-perceived partner responses (beta = 0.16, P = 0.04). After controlling for sexual function and dyadic adjustment, woman-perceived greater solicitous partner responses (beta = 0.16, P = 0.02) predicted greater sexual satisfaction. Partner-perceived responses did not predict women's sexual satisfaction. Partner responses were not associated with women's sexual function. Conclusions. Findings support the integration of dyadic processes in the conceptualization and treatment of PVD by suggesting that partner responses to pain affect pain intensity and sexual satisfaction in affected women.

Attributions about pain as predictors of psychological symptomatology, sexual function, and dyadic adjustment in women with vestibulodynia.
Jodoin M, Bergeron S, Khalifé S, Dupuis MJ, Desrochers G, Leclerc B.
Arch Sex Behav. 2010 Jul 23. [Epub ahead of print]

The present study examined whether attributions for vulvo-vaginal pain predicted pain intensity, sexual function, as well as psychological and dyadic adjustment in women with vestibulodynia. Women with vestibulodynia (N = 77) completed measures of attributions, pain, psychological distress, sexual functioning, and dyadic adjustment. They also took part in a structured interview and a gynaecological examination for diagnostic purposes. Attributions are represented by: (1) internality (personal responsibility) or externality (cause lies in an external situation); (2) globality (entire life affected by the problem) or specificity (problem affecting only a specific situation); (3) stability (problem will still remain in the future) or instability (weak probability that the problem will be maintained with time); and (4) partner responsibility (partner responsible or not for the problem). Results indicated that attributions were not significantly correlated with pain outcomes. However, after controlling for pain intensity and relationship duration, internal attributions predicted higher dyadic adjustment, both global and stable attributions predicted lower dyadic adjustment and higher psychological distress, whereas global attributions also predicted increased sexual impairment. Findings suggest that

cognitive factors, such as attributions, may be related to psychological distress, sexual functioning, and dyadic adjustment in women with vestibulodynia. Results also highlight the importance of adhering to a biopsychosocial perspective focusing on pain reduction, sexual rehabilitation, and relationship enhancement in the treatment of dyspareunia.

Validation of a global pelvic floor symptom bother questionnaire.
Peterson TV, Karp DR, Aguilar VC, Davila GW.
Int Urogynecol J Pelvic Floor Dysfunct. 2010 Sep;21(9):1129-35.

INTRODUCTION AND HYPOTHESIS: This study aimed to validate a symptom questionnaire to assess presence and patient bother as related to common pelvic floor disorders. METHODS: The validation of the Pelvic Floor Bother Questionnaire (PFBQ) included evaluation of internal reliability, test-retest reliability, and validity of the items. RESULTS: A total of 141 patients with mean age of 61.8 +/- 13.2 were included in the study. Twenty-four percent of patients complained of stress urinary incontinence, 14.9% mixed incontinence, 14.9% urge incontinence, 10% fecal incontinence, 5.7% obstructed defecation, 28.4% pelvic organ prolapse, and 2.1% dyspareunia. The PFBQ demonstrated good reliability (alpha = 0.61-0.74; ICC = 0.94). There was a strong agreement beyond chance observed for each question (k = 0.77-0.91). PFBQ correlated with stage of prolapse (rho = 0.73, $p < 0.0001$), number of urinary and fecal incontinence episodes (rho = 0.81, $p < 0.0001$; rho = 0.54, $p < 0.0001$), and obstructed defecation (rho = 0.55, $p < 0.0001$). CONCLUSION: The PFBQ is a useful tool that can be easily used for identification and severity or bother assessment of various pelvic floor symptoms.

Alcock canal syndrome due to obturator internus muscle fibrosis.
Insola A, Granata G, Padua L.
Muscle Nerve. 2010 Sep;42(3):431-2.

Alcock canal syndrome is a rare entrapment neuropathy of the pudendal nerve. We report a case of perineal neuralgia where pudendal nerve compression was due to fibrosis of the obturator internus muscle following an injury of the muscle. After being misdiagnosed for 2 years, the patient was diagnosed only after a combined neurophysiologic and magnetic resonance imaging (MRI) investigation. This case underlines the importance of performing focused neurophysiologic and neuroimaging studies in patients with neuropathic perineal pain in order to reach a correct diagnosis.

Sexual complaints, pelvic floor symptoms, and sexual distress in women over forty.
Knoepp LR, Shippey SH, Chen CC, Cundiff GW, Derogatis LR, Handa VL.
J Sex Med. 2010 Aug 5. [Epub ahead of print]

Introduction. The American Psychiatric Association recommends considering sexually related personal distress when assessing female sexual dysfunction. Currently, there is little data

regarding the impact of sexual complaints on sexual distress. Aim. To investigate the association between sexual complaints and perceived sexual distress in a population of ambulatory adult women. Methods. Using the short forms of the Personal Experiences Questionnaire and Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire, we assessed sexual complaints among 305 women seeking outpatient gynecologic care. Depressive symptoms were quantified using the Center for Epidemiologic Studies Depression (CESD) score. Sexual distress was measured using the Female Sexual Distress Scale (FSDS). Using multivariable logistic regression, we compared sexual complaints between distressed and nondistressed women. Main Outcome Measures. Sexual distress, defined by FSDS score >/=15. Results. FSDS scores were available for 292/305 participants. Seventy-six (26%) scores reflected distress. Distressed women were more likely to be younger (55.2 +/- 1.0 years vs. 56.7 +/- 0.8 years, P = 0.017); have higher CESD scores (16.6 vs. 9.5, P = 0.001); and report decreased arousal (56.8% vs. 25.1%, P = 0.001), infrequent orgasm (54% vs. 28.8%, P = 0.001), and dyspareunia (39.7% vs. 10.6%, P = 0.001). Women with sexual distress were also more likely to report sexual difficulty related to pelvic floor symptoms, including urinary incontinence with sexual activity (9% vs. 1.3%, P = 0.005), sexual avoidance due to vaginal prolapse (13.9% vs. 1%, P = 0.001), or sexual activity restriction due to fear of urinary incontinence (14.9% vs. 0.5%, P = 0.001). After multivariate analysis, sexual distress was significantly associated with dyspareunia (odds ratio [OR] 3.11, P = 0.008) and depression score (OR 1.05, P = 0.006), and inversely associated with feelings of arousal during sex (OR 0.19, P = 0.001). Conclusion. Our results indicate that sexually related personal distress is significantly associated with dyspareunia, depressive symptoms, and decreased arousal during sexual activity. This contributes to our understanding of how sexual complaints may adversely affect women's quality of life.

Pain

The prevalence of chronic pain in United States adults: results of an internet-based survey.
Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH.
J Pain. 2010 Aug 25. [Epub ahead of print]

A cross-sectional, Internet-based survey was conducted in a nationally representative sample of United States (US) adults to estimate the point prevalence of chronic pain and to describe sociodemographic correlates and characteristics of chronic pain. The survey was distributed to 35,718 members (aged 18 years and older) of a Web-enabled panel that is representative of the US population, and 27,035 individuals responded. Crude and weighted prevalence estimates were calculated and stratified by age, sex, and type of chronic pain. The weighted point-prevalence of chronic pain (defined as chronic, recurrent, or long-lasting pain lasting for at least 6 months) was 30.7% (95% CI, 29.8-31.7). Prevalence was higher for females (34.3%) than males (26.7%) and increased with age. The weighted prevalence of primary chronic lower back pain was 8.1% and primary osteoarthritis pain was 3.9%. Half of respondents with chronic pain experienced daily pain, and average (past 3 months) pain intensity was severe (>/=7 on a scale ranging from 0 to 10) for 32%. Multiple logistic regression analysis identified low household

income and unemployment as significant socioeconomic correlates of chronic pain. Chronic pain is prevalent among US adults and is related to indicators of poorer socioeconomic status. PERSPECTIVE: The results of this cross-sectional Internet-based survey suggest a considerable burden of chronic pain in US adults. Chronic pain, experienced by about a third of the population, was correlated with indicators of poorer socioeconomic status. Primary chronic pain was most commonly attributed to lower back pain, followed by osteoarthritis pain.

Variations in brain gray matter associated with chronic pain.
Wood PB.
Curr Rheumatol Rep. 2010 Sep 21. [Epub ahead of print]

Variations in brain gray matter volume and density have been reported in association with a variety of disorders characterized by chronic pain, including chronic low back pain, fibromyalgia, and irritable bowel syndrome. Correlation analyses have demonstrated relationships between morphometric and clinical variables. However, conclusions regarding the nature of these relationships are problematic given that currently available data are derived exclusively from cross-sectional studies. Further efforts to determine the relationship between chronic pain and variations in brain morphometry will depend in part on longitudinal studies of patients at various stages of illness, as well as those at risk of the development of chronic pain. Interpretation of findings from morphometric studies also must take into account genetic and experiential factors that recently have been demonstrated to influence brain morphometry and the risk of developing chronic pain.

Combination drug therapy for chronic pain: a call for more clinical studies.
Mao J, Gold MS, Backonja MM.
J Pain. 2010 Sep 16. [Epub ahead of print]

Chronic pain is a debilitating clinical condition associated with a variety of disease entities including diabetic neuropathy, postherpetic neuralgia, low back pathology, fibromyalgia, and neurological disorders. For many general practitioners and specialists, managing chronic pain has become a daunting challenge. As a modality of multidisciplinary chronic pain management, medications are often prescribed in combinations, an approach referred to as combination drug therapy (CDT). However, many medications for pain therapy, including antidepressants and opioid analgesics, have significant side effects that can compound when used in combination and impact the effectiveness of CDT. To date, clinical practice of CDT for chronic pain has been based largely on clinical experiences. In this article, we will focus on (1) the scientific basis and rationales for CDT, (2) current clinical data on CDT, and (3) the need for more clinical studies to establish a framework for the use of CDT. PERSPECTIVE: More preclinical, clinical, and translational studies are needed to improve the efficacy of combination drug therapy that is an integral part of a comprehensive approach to the management of chronic pain.

A review of SSRIs and SNRIs in neuropathic pain.
Lee YC, Chen PP.
Expert Opin Pharmacother. 2010 Jul 19. [Epub ahead of print]

Importance of the field: Selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs) are becoming increasingly used in the treatment of neuropathic pain and fibromyalgia. However, they are not without adverse effects and their efficacy has not been clear because of conflicting evidence. Areas covered in this review: We have examined the current evidence on the efficacy of SSRIs and SNRIs in the treatment of neuropathic pain and fibromyalgia. Relevant randomized, placebo-controlled studies were identified through a MEDLINE search of English-language literature from January 1990 to December 2009. What the reader will gain: The evidence for efficacy of SSRIs in the treatment neuropathic pain is moderate at best. However, SNRIs, venlafaxine and duloxetine have been shown to be effective in the treatment of painful diabetic neuropathy and polyneuropathy. With fibromyalgia, both SSRIs (fluoxetine and paroxetine) and SNRIs (duloxetine and milnacipran) have been shown to improve pain relief, function and quality of life. Take home message: SSRIs and SNRIs may be considered in the treatment of neuropathic pain if treatment with tricyclic antidepressants and anticonvulsants fails, or if there are contraindications to these drugs. There is also sufficient evidence to indicate that SNRIs are effective in the treatment of fibromyalgia and may be considered early in the treatment of fibromyalgia.

Gender differences in pain modulation by diffuse noxious inhibitory controls: a systematic review.
Popescu A, LeResche L, Truelove EL, Drangsholt MT.
Pain. 2010 Aug;150(2):309-18.

Over the last decade, extensive research has demonstrated sex differences in pain perception and modulation. Several factors have been proposed to account for the differences observed between men and women, including pain modulation through diffuse noxious inhibitory controls (DNIC). Studies investigating sex differences in DNIC have shown mixed results, with some reporting decreased DNIC effect in women compared with men, while others found no difference in DNIC between the sexes. Additional studies have investigated DNIC in both sexes without focusing on sex differences. This systematic review aimed to answer the following question: "In humans of reproductive age without chronic pain, are women more likely than men to have decreased Diffuse Noxious Inhibitory Controls?" Relevant studies were identified by computerized searches of Pubmed/Medline, Embase, Biosis, Web of Science, PsycInfo and Cochrane (from January 1980 through February 2009). The search was limited to human studies with no language restriction. The initial search identified 718 titles and abstracts. Seventeen studies were included in the final stage and data regarding age and gender of participants, methodology and outcome measurements were extracted and analyzed. The majority of studies using pain report as the outcome found significantly more efficient DNIC in males than females (mean female/male ratio=0.54). Studies evaluating pain thresholds and nociceptive flexion reflex indicated the opposite when simply averaged across studies; however, weighted

analyses of threshold found more efficient DNIC in males. Gender differences in DNIC effect depend on both the experimental methodology and the modes of measurement of the effect.

Sex differences in hypothalamic-pituitary-adrenal axis function in patients with chronic pain syndrome.
Turner-Cobb JM, Osborn M, da Silva L, Keogh E, Jessop DS.
Stress. 2010 Jul;13(4):292-300.

Chronic pain is often equated with chronic stress yet the relationship between chronic pain and hypothalamic-pituitary-adrenal (HPA) axis activity is poorly understood. The objective of this study was to examine diurnal functioning of the HPA axis in patients with clinically defined non-inflammatory chronic pain syndrome (CPS) compared to controls. The sample consisted of 37 adults with CPS and 47 healthy controls. All participants provided saliva samples at awakening, 12:00, 18:00 and 21:00 h on two consecutive days, as well as completing self-report questionnaires relating to anxiety and depression. The CPS group had a significantly lower overall mean diurnal salivary cortisol concentration compared to the control group ($p < 0.01$) but no significant differences were found between the two groups for repeated cortisol sampling across the day. However, a three-way interaction of time of day by patient status by sex was found ($p < 0.032$), with lower cortisol concentration in male patients compared to female patients in the afternoon period. No significant group effect was found for the rate of decline in the circadian rise in cortisol concentration. These data demonstrate that CPS is associated with a degree of hypocortisolemia, particularly in male patients. The altered dynamics of cortisol secretion in CPS in relation to the onset and duration of pain in patients remains to be determined.

Acid-sensing ion channels (ASICs): pharmacology and implication in pain.
Deval E, Gasull X, Noël J, Salinas M, Baron A, Diochot S, Lingueglia E.
Pharmacol Ther. 2010 Aug 31. [Epub ahead of print]

Tissue acidosis is a common feature of many painful conditions. Protons are indeed among the first factors released by injured tissues, inducing a local pH fall that depolarizes peripheral free terminals of nociceptors and leads to pain. ASICs are excitatory cation channels directly gated by extracellular protons that are expressed in the nervous system. In sensory neurons, they act as "chemo-electrical" transducers and are involved in somatic and visceral nociception. Two highly specific inhibitory peptides isolated from animal venoms have considerably helped in the understanding of the physiological roles of these channels in pain. At the peripheral level, ASIC3 is important for inflammatory pain. Its expression and its activity are potentiated by several pain mediators present in the "inflammatory soup" that sensitize nociceptors. ASICs have also been involved in some aspects of mechanosensation and mechanonociception, notably in the gastrointestinal tract, but the underlying mechanisms remain to be determined. At the central level, ASIC1a is largely expressed in spinal cord neurons where it has been proposed to participate in the processing of noxious stimuli and in central sensitization. Blocking ASIC1a in

the spinal cord also produces a potent analgesia in a broad range of pain conditions through activation of the opiate system. Targeting ASIC channels at different levels of the nervous system could therefore be an interesting strategy for the relief of pain.

H3 receptor miniseries: H3 receptors and pain modulation: peripheral, spinal and brain interactions.
Hough L, Rice FL.
J Pharmacol Exp Ther. 2010 Sep 23. [Epub ahead of print]

Histamine H(3) receptors (H(3)Rs), distributed within in the brain, the spinal cord, and on specific types of primary sensory neurons, can modulate pain transmission by several mechanisms. In the skin, H(3)Rs are found on certain Aβ fibers, and on keratinocytes and Merkel cells, as well as on deep dermal, peptidergic Aδ fibers terminating on deep dermal blood vessels. Activation of H(3)Rs on the latter in the skin, heart, lung and dura mater reduces CGRP and substance P release, leading to anti-inflammatory (but not antinociceptive) actions. However, activation of H(3)Rs on the spinal terminals of these sensory fibers reduces nociceptive responding to low intensity mechanical stimuli, and to inflammatory stimuli such as formalin. These findings suggest that H(3)R agonists might be useful analgesics, but these drugs have not been tested in clinically-relevant pain models. Paradoxically, H(3) antagonists/ inverse agonists have also been reported to attenuate several types of pain responses, including phase II responses to formalin. In the periaquaductal gray (PAG, an important pain regulatory center), the H(3) inverse agonist thioperamide releases neuronal histamine and mimics histamine's biphasic modulatory effects in thermal nociceptive tests. Newer H(3) inverse agonists with potent, selective, and brain-penetrating properties show efficacy in several neuropathic and arthritis pain models, but the sites and mechanisms for these actions remain poorly understood.

KST5468, a new T-type calcium channel antagonist, has an antinociceptive effect on inflammatory and neuropathic pain models.
Lee MJ, Shin TJ, Lee JE, Choo H, Koh HY, Chung HJ, Pae AN, Lee SC, Kim HJ.
Pharmacol Biochem Behav. 2010 Aug 3. [Epub ahead of print]

The T-type Ca(2+) channel is a low-voltage-activated Ca(2+) channel related to nociceptive stimuli. Increases in Ca(2+) due to calcium channel activation enhance pain sensitivity through both peripheral and central pain pathways. We have developed a novel compound, KST5468, which is a T-type calcium channel antagonist. The new synthetic compound may have an antinociceptive effect, and thus we evaluated KST5468 as a putative analgesic in a hot plate test, a formalin test, and two neuropathic pain models. KST5468 caused a significant increase in latency in the hot plate test at 30min after a 10mg/kg peritoneal injection of the compound. Interestingly, in the second phase of formalin test, KST5468 decreased pain behaviors in a dose-dependent manner. Moreover, in two neuropathic pain models induced by chronic constriction

and spared nerve injury, KST5468 significantly increased the mechanical pain threshold. Using immunohistochemistry, expression of two well known pain-related molecular markers, c-Fos and calcitonin gene-related peptide (CGRP), and phosphorylated extracellular signal-related kinase (p-ERK) were found to be decreased in the laminae I-II layers of the ipsilateral L4-L5 spinal dorsal horn in KST5468 treated mice. Taken together, the results of this study suggest that KST5468 may be an effective antinociceptive agent for neuropathic pain.

Targeting TRPV1 as an alternative approach to narcotic analgesics to treat chronic pain conditions.
Premkumar LS.
AAPS J. 2010 Sep;12(3):361-70.

In spite of intense research efforts and after the dedicated Decade of Pain Control and Research, there are not many alternatives to opioid-based narcotic analgesics in the therapeutic armamentarium to treat chronic pain conditions. Chronic opioid treatment is associated with sedation, tolerance, dependence, hyperalgesia, respiratory depression, and constipation. Since the affective component is an integral part of pain perception, perhaps it is inevitable that potent analgesics possess the property of impacting pain pathways in the supraspinal structures. The question still remains to be answered is that whether a powerful analgesic can be devoid of narcotic effect and addictive potentials. Local anesthetics are powerful analgesics for acute pain by blocking voltage-gated sodium channels that are involved in generation and propagation of action potentials. Antidepressants and anticonvulsants have proven to be useful in the treatment of certain modalities of pain. In neuropathic pain conditions, the complexity arises because of the notion that neuronal circuitry is altered, as occurs in phantom pain, in that pain is perceived even in the absence of peripheral nociceptive inputs. If the locus of these changes is in the central nervous system, commonly used analgesics may not be very useful. This review focuses on the recent advances in nociceptive transmission and nociceptive transient receptor potential vanilloid 1 channel as a target for treating chronic pain conditions with its agonists/antagonists.

Other Vulvovaginal Disorders

The effect of vulvar lichen sclerosus on quality of life and sexual functioning.
Van De Nieuwenhof HP, Meeuwis KA, Nieboer TE, Vergeer MC, Massuger LF, De Hullu JA.
J Psychosom Obstet Gynaecol. 2010 Aug 11. [Epub ahead of print]

Lichen sclerosus (LS) is a chronic skin disorder mostly seen on the female anogenital skin. The aim of this study was to evaluate the quality of life (QoL) and sexuality in female patients with LS and to compare their scores with healthy controls. In addition, we wanted to find factors associated with impaired sexual functioning in patients with LS. Members of the Dutch LS

foundation and support group were asked to fill in three questionnaires: the Dermatology Quality of Life Index, Female Sexual Function Index (FSFI) and Female Sexual Distress Scale (FSDS). 215 of 368 patients returned their questionnaire (58.4%). Their scores were compared to a control group which consisted of 61 women of similar age ($p = 0.472$) without a skin disorder. Of all domains of QoL, LS interfered most with sexual functioning. Patients significantly scored lower on all subscales of the FSFI (desire ($p = 0.016$), arousal ($p < 0.001$), lubrication ($p < 0.001$), orgasm ($p < 0.001$), satisfaction ($p < 0.001$) and pain ($p < 0.001$), indicating worse sexual functioning. These problems with sexual functioning brought about significant sexual distress ($p < 0.001$). Patients who experienced more influence on their QoL had more sexual difficulties, leading to more sexual distress independent of their age.

Efficacy of photodynamic therapy in vulvar lichen sclerosus treatment based on immunohistochemical analysis of CD34, CD44, myelin basic protein, and Ki67 antibodies.
Olejek A, Steplewska K, Gabriel A, Kozak-Darmas I, Jarek A, Kellas-Sleczka S, Bydliński F, Sieroń-Stołtny K, Horak S, Chełmicki A, Sieroń A.
Int J Gynecol Cancer. 2010 Jul;20(5):879-87.

INTRODUCTION: Lichen sclerosus (LS) is a chronic skin and mucosa inflammatory disease. It affects mainly the female anogenital area especially in postmenopausal period. The main symptoms include pruritus, burning, pain, sometimes urinary problems, or difficulties in defecation. Usually, porcelain-white plaques are seen in the skin and mucosa. The etiology and pathogenesis of LS are still uncertain. There are some research studies on possible genetic predisposition, yet autoimmune, hormonal, or infectious factors are not excluded. The typical treatment of LS is mainly pharmacological, although the alternative treatment method used in LS is photodynamic therapy (PDT), which is noninvasive technique based on selective destruction of lesions. Our study is focused on molecule markers of vascularisation (CD34), nervous cell function (myelin basic protein [MBP]), keratinocyte function (CD44), and proliferation index (Ki67) in cases treated with photodynamic method. MATERIALS AND METHODS: A group of 100 patients treated in our department was included in the study. All 100 women had LS on the basis of clinical and histological criteria. All the subjects underwent PDT. In all cases, skin biopsies were taken before and after treatment, and samples were analyzed with CD34, CD44, MBP, and Ki67 antibodies using immunohistochemical staining. RESULTS: The study shows the high efficacy of PDT in LS treatment including beneficial changes to CD34, CD44, and MBP immunostained molecules. The Ki67 proliferation index did not change significantly. A significant increase of CD34 (microvessel density), MBP, and CD44 expression was confirmed in the histological images and in the partial or full remission of clinical objective and subjective symptoms. CONCLUSIONS: The PDT is a very effective therapeutic method in LS treatment.

Differential hypermethylation of genes in vulvar cancer and lichen sclerosus coexisting or not with vulvar cancer.

Guerrero D, Guarch R, Ojer A, Casas JM, Méndez-Meca C, Esteller M, Barba-Ramos E, Garcia-Bragado F, Puras A.

Int J Cancer. 2010 Aug 23. [Epub ahead of print]

Squamous cell carcinoma of the vulva is a heterogeneous disease, associated or not with vulvar lichen sclerosus (LS). The precursor role of LS in vulvar cancer is unclear. We studied the epigenetic alterations of RASSF1A, RASSF2A, p16, TSP-1 and MGMT genes in vulvar squamous cell carcinomas (SCC), LS associated with SCC, isolated LS and normal vulvar skin. Gene hypermethylation and human papillomavirus (HPV) presence were evaluated by methylation-specific PCR and PCR/reverse line blot, respectively. High-risk HPV types were present in 16.7% of the vulvar SCC patients. There were increasing percentages of hypermethylation of genes from isolated LS to LS associated with vulvar SCC and vulvar SCC. The genes were hypermethylated more frequently in vulvar SCC associated with LS than in those not associated with LS, MGMT and RASSF2A being unmethylated in LS not associated with vulvar SCC. TSP-1 hypermethylation was related to recurrence in patients with vulvar cancer. Conclusions: (I) The epigenetic inactivation of genes is a common event in vulvar SCC and is also present in adjacent lesions, implying a possible precursor role for these alterations. (II) MGMT and RASSF2-A hypermethylation are present exclusively in vulvar SCC and LS associated with SCC, and absent from isolated LS. (III) TSP-1 hypermethylation is a bad prognosis factor in vulvar SCC.

Vulval lichen sclerosus and lichen planus.

McPherson T, Cooper S.

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Lichen sclerosus (LS) and lichen planus (LP) are both immunologically mediated diseases with a preference for the genitalia. The basic principles of management of vulval LS and vulvovaginal LP are the same and involve explanation of the disease, emphasizing the chronic nature of the condition and outlining treatment options. The main difference between the two conditions is that LP has a propensity to involve the mucous membranes including the mouth and vagina which are rarely affected in LS. First-line treatment for LS is a super-potent topical corticosteroid ointment which has a high response rate. Erosive vulvovaginal LP is more challenging to treat. Second-line therapies include topical calcineurin inhibitors and systemic agents. There is limited evidence for systemic treatments for both conditions. The risk of vulval squamous cell carcinoma (SCC) is increased in both LP and LS, and it is not known how treatment affects this risk. We recommend teaching self-examination and longitudinal evaluation.

Vaginal involvement in genital erosive lichen planus.
Helgesen AL, Gjersvik P, Jebsen P, Kirschner R, Tanbo T.
Acta Obstet Gynecol Scand. 2010 Jul;89(7):966-70.

A specialized Vulva Clinic with dedicated gynecologists and dermatologists was established in Oslo, Norway, in 2003. Fifty-eight women referred to the clinic in 2003-2009 were diagnosed with genital erosive lichen planus. All patients filled out a questionnaire. Gynecological examination, including vaginal inspection, was performed, if necessary in general anesthesia. Median age at symptom start was 51 years (range 17-78 years) with 15 women (26%) being younger than 40 years old. Sexual abstinence was reported by 36 women and dyspareunia by another 10. On examination, vaginal involvement was seen in 49 women, including vaginal synechiae in 29 and total obliteration of the vagina in 9. Of 56 women treated with topical corticosteroids for at least three months, two had complete response and 36 partial responses. Similarly, of 22 women treated with tacrolimus, three had complete and six partial response. We conclude that vaginal involvement is more common in genital erosive lichen planus than previously reported.

Pigmented vulvar lesions.
Edwards L.
Dermatol Ther. 2010 Sep;23(5):449-457.

Pigmented lesions represent an enormous range of conditions, from benign to malignant tumors, and from infectious to post-inflammatory. Pigmented lesions are much less easily diagnosed on anogenital skin, and clinicians should have a low threshold for biopsy confirmation of diseases not classic in appearance.

Atrophic vaginitis.
Stika CS.
Dermatol Ther. 2010 Sep;23(5):514-522.

With the loss of estrogen that occurs with menopause, physiologic and structural changes occur within the vulvovaginal mucosa that lead to a condition commonly called atrophic vaginitis. Although mild genital changes occur in most women, 10-47% of postmenopausal women will develop one or more debilitating symptoms that include vulvovaginal dryness, dyspareunia, vulvar itching or pain, recurrent urinary tract infections, as well as abnormal vaginal discharge. Topical estrogen replacement therapies reverse these mucosal changes and are effective treatments for the symptoms of atrophic vaginitis. Vaginal moisturizers and lubricants also provide symptomatic relief for vaginal dryness and dyspareunia, respectively.

Candida albicans forms biofilms on the vaginal mucosa.
Harriott MM, Lilly EA, Rodriguez TE, Fidel PL, Noverr MC.
Microbiology. 2010 Aug 12. [Epub ahead of print]

Current understanding of resistance and susceptibility to vulvovaginal candidiasis (VVC) challenges existing paradigms of host defense against fungal infection. While abiotic biofilm formation has a clearly established role during systemic Candida infections, it is not known whether C. albicans forms biofilms on the vaginal mucosa and their role in disease. In vivo and ex vivo murine vaginitis models were employed to examine biofilm formation by scanning electron and confocal microscopy. C. albicans strains included 3153A (lab strain), DAY185 (parental control strain), and mutants defective in morphogenesis and/or biofilm formation in vitro (efg1/efg1 and bcr1/bcr1). Both 3153A and DAY815 formed biofilms on the vaginal mucosa in vivo and ex vivo as indicated by high fungal burden and microscopic analysis demonstrating typical biofilm architecture and presence of extracellular matrix (ECM) co-localized with the presence of fungi. In contrast, efg1/efg1 and bcr1/bcr1 mutant strains exhibited weak to no biofilm formation/ECM production in both models compared to wildtype strains and complemented mutants despite comparable colonization levels. These data show for the first time that C. albicans forms biofilms on in vivo on vaginal epithelium, and that in vivo biotic biofilm formation requires regulators of biofilm formation (BCR1) and morphogenesis (EFG1).

Evaluation of risk factors in patients with vulvovaginal candidiasis and the value of chromID Candida agar versus CHROMagar Candida for recovery and presumptive identification of vaginal yeast species.
Guzel AB, Ilkit M, Akar T, Burgut R, Demir SC.
Med Mycol. 2010 Jul 7. [Epub ahead of print]

Vulvovaginal candidiasis (VVC), particularly the recurrent form, remains an intractable problem for clinicians, microbiologists, and patients. It is essential to confirm the clinical diagnosis by mycological methods and avoid empirical therapy. The recovery of yeast in fungal culture, such as on Sabouraud dextrose agar, remains the gold standard for diagnosis. In this investigation, we examined 474 participants, including 122 (25.7%) with acute VVC cases, 249 (52.5%) who had recurrent VVC (RVVC) cases, and 103 (21.7%) healthy controls. We also administered a questionnaire to obtain information on patient lifestyle and medical, gynecological, and sexual history. In addition, we compared the performance of chromID Candida agar (CAN2) to CHROMagar Candida (CAC) and Sabouraud dextrose agar with gentamicin and chloramphenicol (SGC2). The yeasts were identified by conventional methods including the germ tube test, microscopic morphology on cornmeal-Tween 80 agar, and the commercial API 20C AUX system. We detected yeasts in 60 of 122 (49.2%) patients with acute VVC cases, 110 of 249 (44.2%) with RVVC cases, and in 35 of 103 (34%) healthy controls (P = 0.07). A total of 205 samples were found to be positive for fungi (43.2%), of which 176 (85.9%) were monofungal, and 29 (14.1%) were polyfungal. In addition, 198 of these samples (96.6%) were positive on CAN2, 195 (95.1%) on CAC, 189 (92.2%) on SGC2, and 183 (89.3%) samples on all three (P = 0.17). The 234 yeast

isolates recovered were C. albicans (n = 118), C. glabrata (n = 82), C. kefyr (n = 11), C. krusei (n = 9), C. lipolytica (n = 3), C. colliculosa (n = 2), C. parapsilosis (n = 2), C. pelliculosa (n = 2), C. tropicalis (n = 2), and other species of Candida (n = 3). Of the 29 polyfungal populations, 28 (96.6%) were detected in CAN2, 25 in (86.2%) CAC, and 25 (86.2%) on both (P = 0.35). Notably, we detected the high predominance of C. albicans+C. glabrata (86.2%) in polyfungal populations. Briefly, the detection of C. albicans after 24 h of incubation was easier on CAN2 (64.4%) than on CAC (25.4%). This study showed that CAN2 is a rapid and reliable medium for immediate identification of C. albicans and for detecting polyfungal populations in vaginal specimens. We observed that the use of antibiotics, intrauterine devices, as well as, perineal laceration, short anovaginal distance (< 3 cm), and genital epilation in common areas are predisposing factors for RVVC (P < 0.001). In addition, we detected that the use of menstrual pad, using an (IUD), and having a history of childbirth increased the risk of both acute and recurrent VVC (P < 0.01), whereas the use of a daily pad and walking daily significantly decreased the risk of both acute and recurrent VVC (P < 0.01).

Management of postmenopausal vaginal symptoms in women.
Bond S, Horton LS.
J Gerontol Nurs. 2010 Jul;36(7):3-7.

Although menopause is a normal, physiological process in the lives of women, many report uncomfortable urogenital symptoms as they transition through this stage. Such symptoms include urinary frequency, increased urinary tract infections, vaginal dryness and irritation, and painful intercourse, among others. While each of these symptoms presents unique challenges for clinicians, this article specifically focuses on the management of vaginal symptoms. A thorough medical history, physical examination, and laboratory testing assist in confirming a diagnosis and selecting a treatment plan. A careful and detailed discussion with women to elicit their knowledge and concerns about the use and risks of hormone therapy prior to initiation can avoid misunderstanding, improve adherence, and enhance quality of life.

Nursing considerations in patients with vaginitis.
Holloway D.
Br J Nurs. 2010 Sep 9;19(16):1040-6.

Vaginitis is defined as an inflammation of the vagina. It can result in symptoms of any or all of the following: discharge, itching and pain, and often irritation or infection of the vulva. There is no specific cause for vaginitis, and many other conditions can cause the symptoms. Vaginitis is a distressing condition that affects many women of reproductive age and beyond, and encompasses candidiasis (also known as thrush), bacterial vaginosis, and trichomoniasis. It can occur in a single episode, or recur throughout a woman's lifetime. Some women will seek medical help, but many more self-treat with over-the-counter medications, suspecting the reoccurrence of Candida in particular. This article aims to explore the causes, signs and

symptoms, and treatments of vaginitis to provide nurses with the necessary background information to feel more confident in dealing with women's health issues.

Distribution of human papillomavirus types in the anogenital tract of females and males.
Barzon L, Militello V, Pagni S, Franchin E, Dal Bello F, Mengoli C, Palù G.
J Med Virol. 2010 Aug;82(8):1424-30.

Human papillomavirus (HPV) infection is the most common sexually transmitted infection in both men and women, but there are limited data comparing the prevalence of HPV infection between genders and in different anogenital sites. This cross-sectional analysis describes the distribution of HPV types in the genital tract of 3,410 consecutive females and 1,033 males undergoing voluntary screening for HPV and referred to a single institution. The relationship between specific HPV types and the presence of anogenital lesions was examined. In both females and males, the overall prevalence of HPV infection was about 40%. A wide variety of HPV types was identified, but the prevalence of different types was remarkably similar in the two genders, even when considering different anatomical sites. HPV-6 was the most frequent (prevalence 13%) type in all anogenital sites in men followed by HPV-16 (7%), while HPV-16 was the most common type in women (about 6%), either in the cervix, vagina, or vulva, followed by HPV-6. In addition to HPV-16, HPV-58, HPV-33, HPV-31, and HPV-56 were the carcinogenic types detected most commonly and were significantly associated with high-grade squamous intraepithelial cervical lesions, while HPV-53 and HPV-66 were the most common among possibly carcinogenic types. In both genders, anogenital warts were associated with HPV-6 and HPV-11 infection, and, less frequently, with other types, like HPV-54, HPV-62, and HPV-66. These results show that genital HPV infection involves numerous HPV types, which have similar distribution patterns in females and males and in different anogenital anatomical sites

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None.