

NVA Research Update E-Newsletter

June 2011

www.nva.org

This newsletter has been supported, in part, through a grant from the
Enterprise Holdings Foundation.

<http://enterpriseholdings.com/>
www.enterprise.com

This newsletter is quarterly and contains abstracts from medical journals published between March and June 2011. Abstracts presented at scientific meetings may also be included. Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia / Vulvovaginal Pain

Altered central sensitization in subgroups of women with vulvodynia.

Zhang Z, Zolnoun DA, Francisco EM, Holden JK, Dennis RG, Tommerdahl M
Clin J Pain. 2011 May 17. [Epub ahead of print]

OBJECTIVE: To investigate the clinical correlates of central nervous system alterations among women with vulvodynia. Altered central sensitization has been linked to dysfunction in central nervous system-inhibitory pathways (eg, γ -aminobutyric acidergic), and metrics of sensory adaptation, a centrally mediated process that is sensitive to this dysfunction, could potentially be used to identify women at risk of treatment failure using conventional approaches.

METHODS: Twelve women with vulvodynia and 20 age-matched controls participated in this study, which was conducted by sensory testing of the right hand's index and middle fingers. The following sensory precepts were assessed: (1) vibrotactile detection threshold; (2) amplitude discrimination capacity (defined as the ability to detect differences in intensity of simultaneously delivered stimuli to 2 fingers); and (3) a metric of adaptation (determined by the impact that applying conditioning stimuli have on amplitude discriminative capacity). **RESULTS:** Participants did not differ on key demographic variables, vibrotactile detection threshold, and amplitude discrimination capacity. However, we found significant differences from controls in adaptation metrics in 1 subgroup of vulvodynia patients. Compared with healthy controls and women with a shorter history of pain [$n=5$; duration (y)= 3.4 ± 1.3], those with a longer history [$n=7$; duration (y)= 9.3 ± 1.4] were found to be less likely to have adaptation metrics similar to control values. **DISCUSSION:** Chronic pain is thought to lead to altered central sensitization, and adaptation is a centrally mediated process that is sensitive to this condition. This report suggests that similar alterations exist in a subgroup of vulvodynia patients.

Differences in primary compared with secondary vestibulodynia by immunohistochemistry.

Leclair CM, Goetsch MF, Korcheva VB, Anderson R, Peters D, Morgan TK
Obstet Gynecol. 2011 Jun;117(6):1307-13.

OBJECTIVE: To assess whether primary and secondary vestibulodynia represent different pathologic pathways. **METHODS:** This was an analysis of archived vestibulectomy specimens from 88 premenopausal women with vestibulodynia (2002-2008). Patient records were reviewed to classify the type of vestibulodynia, duration of symptoms, and hormone status. Histologic sections were stained for hematoxylin and eosin to grade inflammation, S100 to highlight nerves, CD117 for mast cells, estrogen receptor α , and progesterone receptor. Differences between primary and secondary vestibulodynia were tested by t tests, chi-square analysis, and linear and logistic regression. **RESULTS:** Primary vestibulodynia showed significant neural hypertrophy and hyperplasia ($P=.02$, adjusted odds ratio [OR] 3.01, 95% confidence interval [CI] 1.2-7.6) and increased progesterone receptor nuclear immunostaining ($P=.004$, adjusted OR 3.94, CI 1.6-9.9) compared with secondary vestibulodynia. Estrogen receptor α expression was also greater in primary vestibulodynia when symptom diagnosis was less than 5 years ($P=.004$, adjusted OR 5.53 CI 1.71-17.91). **CONCLUSION:** Primary and secondary vestibulodynia have significantly different histologic features, suggesting that they may have separate mechanistic pathways. Clinically, this may mean the discovery of distinct conditions.

Measuring treatment outcomes in women with vulvodynia.

Ventolini G

J Clin Med Res. 2011;3(2):59-64.

Full text: <http://www.jocmr.org/index.php/JOCMR/article/viewArticle/526/300>

Vulvodynia or vulvar pain syndrome is a chronic, heterogeneous, and multifactorial gynecological condition with an estimated prevalence of 9 - 12%, broad and substantial effect on quality of life due to physical disabilities, psychological distress and sexual dysfunction. A rationale therapeutic approach for the treatment of vulvodynia is still under investigation. A review of treatment modalities proposed by most of the clinicians involved in managing these patients advocated initially utilizing non-invasive therapies and then to proceed gradually to more aggressive therapies. A multidisciplinary approach that includes behavioral science and neuroimaging is required and recommended. Additionally a team approach should be utilized to test and evaluate therapies including pelvic floor physiotherapy, psychotherapy, microbiology and pharmacology. It is my hope that this review will assist in the understanding of vulvodynia and its measuring treatment outcomes and will provide a thrust in the right direction to once and for all clarify this complex multifactorial disorder affecting women.

Vulvodynia in adolescence: childhood vulvar pain syndromes.

Clare CA, Yeh J

J Pediatr Adolesc Gynecol. 2011 Jun;24(3):110-5.

BACKGROUND: Children, adolescents and young women represent a unique group of patients with vulvodynia. **STUDY OBJECTIVE:** To define and characterize vulvodynia, diagnostic criteria, causes and pathophysiology, propose treatment modalities, emphasizing its prevalence in young children, adolescents and young women less than 25 years of age. **DESIGN:** Medline review of the literature on vulvar pain disorders, using the key word vulvodynia, from the years 1995 to 2010, comparing characteristics in children, adolescents and young women ages 25 years and less to older adult women. **SETTING:** MEDLINE review of current literature from 1995 to 2010. **PARTICIPANTS:** None **INTERVENTIONS:** There were no interventions during this literature review. **MAIN OUTCOME MEASURES:** A synthesis of cases of vulvodynia in these populations and the specific characteristics and recommendations in these age groups. **RESULTS:** Childhood vulvar pain is usually found to have a cause. Pain characteristics in this group are similar to adults. In adolescents and young reproductive age women, vulvar pain is associated with sexual intercourse or early tampon use. The psychological component of vulvar pain is limited due to small numbers of patients available for review. Treatment modalities and recommendations are based on limited data. **CONCLUSIONS:** Women with vulvodynia vary in ages from 16 to 80 years with the majority between the ages of 20 to 50 years. Young women in their teens and early twenties are at the greatest risk of developing vulvodynia. Vulvar pain disorders are important in these groups because early pain syndromes may affect future development of body image, self-esteem, and attitudes toward sexual behavior and functioning.

The causes and prevalence of vestibulodynia: a vulvar pain disorder.

Feldhaus-Dahir M

Urol Nurs. 2011 Jan-Feb;31(1):51-4.

Vestibulodynia is a chronic type of vulvar pain that affects at least 16% of women in the United States. The condition is often misdiagnosed or not diagnosed at all due to a lack of knowledge among health care professionals. Delayed diagnosis puts a woman at risk for sexual dysfunction, decreased quality of life, and relationship conflict.

Intralevator injection of botulinum toxin for the treatment of hypertonic pelvic floor muscle dysfunction and vestibulodynia.

Goldstein AT, Burrows LJ, Kellogg-Spadt S.

J Sex Med. 2011 May;8(5):1287-90. doi: 10.1111/j.1743-6109.2011.02270.x

No abstract available.

Interstitial cystitis is associated with vulvodynia and sexual dysfunction - a case-control study.

Gardella B, Porru D, Nappi RE, Daccò MD, Chiesa A, Spinillo A.

J Sex Med. 2011 Jun;8(6):1726-34. doi: 10.1111/j.1743-6109.2011.02251.x.

Introduction. Dyspareunia and sexual dysfunction are common in women with urological disorders. The study of comorbidity between interstitial cystitis (IC) and vulvodynia seems to be relevant to understand the mechanism generating pain in these conditions. **Aim.** To conduct a case-control study for evaluating vulvodynia and sexual dysfunction in women with IC.

Methods. Forty-seven women with new diagnosis (National Institutes of Health [NIH]/National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK] Criteria) of IC were compared with 188 age-matched, negative controls. Each woman completed a semi-structured interview and the Female Sexual Function Index (FSFI). A gynecological examination to assess vulvodynia (cotton swab testing) and genital health (vulvoscopy, Pap smear, culture, and vaginal health index score [VHIS]) was performed. **Main Outcome Measures.** Prevalence of vulvodynia, sexual function, and sociodemographic/gynecological variables significantly associated with IC.

Results. Spontaneous or provoked vulvodynia was reported by 23.4% and 74.5% of IC cases, respectively. Sexual function was significantly impaired (median total FSFI score: IC cases 16.85 ± 8.73 vs. controls 27.34 ± 6.41 ; $P < 0.0001$) in sexually active women, and 23.4% of IC cases as compared to 9% of controls reported no sexual activity in the year preceding the study (χ^2 for trend = 38.2, $P < 0.0001$). VHIS was highly impaired in women with IC in comparison with controls ($P < 0.0001$). Variables significantly associated with IC were a diagnosis of menopause (odds ratio [OR] = 31.2, 95% confidence interval [CI] = 8.1-120.5), past (OR = 4.6, 95% CI = 1.74-12.1) or current (OR = 6.9, 95% CI = 2.1-22.1) oral contraceptive use, and a histologically confirmed diagnosis of endometriosis (OR = 3.7, 95% CI = 1.1-12.7). **Conclusion.** We found an increased prevalence of vulvodynia among women with recently diagnosed IC; both conditions seem to have profound consequences on women's sexual function. A potential role for sex hormone-dependent mechanisms into the comorbidity of vulvar and bladder pain is proposed, but further research is warranted.

Psychosexual correlates of persistent postsurgical pain in patients with vulvodynia.

Eanes A, Bair E, Martin C, Iyer P, Zolnoun D

Int J Gynaecol Obstet. 2011 Jun;113(3):225-8.

OBJECTIVE: To examine long-term reports of pain and psychologic correlates of pain in women after vestibulectomy. **METHODS:** In a retrospective cross-sectional exploratory study, 37 women who had undergone vestibulectomy between January 1989 and January 2008 completed questionnaires assessing demographic information, self-reported levels of pain, anxiety, somatization, psychologic distress, and sexual function. **RESULTS:** Eight women reported being completely pain free after surgery. The remaining 29 women reported various levels of pain during intercourse (as measured by the Gracely pain scale) and decreased sexual function (as measured by a sexual functioning questionnaire). Various measures of psychologic distress were associated with average intercourse-related pain, including brief symptom inventory ($P=0.002$), Pennebaker inventory of limbic languidness ($P=0.002$), perceived stress

scale ($P=0.04$), and Spielberger trait-anxiety inventory ($P=0.01$). These same measures of psychological distress were similarly associated with general, unprovoked vaginal pain.
CONCLUSION: The present data suggest that the pathophysiology of localized vulvodynia may be more complex in some women, leading to a suboptimal response to surgical treatment.

Risk factors for chronic pelvic pain in a cohort of primipara and secondipara at one year after delivery: association of chronic pelvic pain with autoimmune pathologies.

Driul L, Bertozzi S, Londero AP, Fruscalzo A, Rusalen A, Marchesoni D, Di Benedetto P
Minerva Ginecol. 2011 Apr;63(2):181-7.

AIM: Over genetic and obstetric factors, also autoimmunity may be involved in female chronic pelvic pain (CPP) pathogenesis. Our study aims to determinate the prevalence of CPP after one year from delivery, and to investigate the possible influence on CPP of concomitant autoimmune conditions. **Methods.** We selected a cohort of caucasian primipara and secondipara who delivered in our clinic in 2006. We collected personal, clinical and obstetric data, and asked them about pelviperineal painful symptoms. **Results.** Mean maternal age is 35.52 years (± 4.70), 27.65% of women delivered by cesarean section, 61.04% spontaneously and 11.32% by operative assistance, with partoanalgesia in 10.39% of cases, episiotomy in 41.19%, vaginoperineal tears in respectively 14.10% I degree, 11.13% II degree and 0.93% III-IV degree; 43.60% of women have ever undergone abdominopelvic surgery, 32.84% by laparotomy-laparoscopy, 7.05% by hysteroscopy, 5.01% limited to perineum. Chronic autoimmune diseases affect 78.48% of women, allergies 7.79%, rheumatic pathologies 1.3%, autoimmune endocrinopathies 71.8%; 26.53% of women report pelviperineal painful symptoms, being already present in 2.23% of cases, 12.43% generalised pelvic pain, 4.27% bladder pain, 2.60% vulvodynia, 17.07% dyspareunia. By monovariate analysis CPP results influenced by III-IV degree vaginoperineal tears, operative assistance, preexisting CPP, previous and actual urinary incontinence, previous abdominopelvic surgical interventions and chronic rheumatic pathologies. Furthermore, rheumatic disease, operative assistance and previous CPP are predictive factors for CPP in the postpartum ($AUC=58.10\%$). **Conclusion.** Delivery may highlight CPP symptoms in predisposed women affected by chronic autoimmune pathologies.

Chronic female pelvic pain—part 1: Clinical pathoanatomy and examination of the pelvic region.

Apte G, Nelson P, Brismee J, Dedrick G, Justiz III R, Sizer Jr PS.
Pain Practice. Epub ahead of print May 26, 2011

Chronic pelvic pain is defined as the presence of pain in the pelvic girdle region for over a 6-month period and can arise from the gynecologic, urologic, gastrointestinal, and musculoskeletal systems. As 15% of women experience pelvic pain at some time in their lives with yearly direct medical costs estimated at \$2.8 billion, effective evaluation and management strategies of this condition are necessary. This merits a thorough discussion of a systematic approach to the evaluation of chronic pelvic pain conditions, including a careful history-taking

and clinical examination. The challenge of accurately diagnosing chronic pelvic pain resides in the degree of peripheral and central sensitization of the nervous system associated with the chronicity of the symptoms, as well as the potential influence of the affective and biopsychosocial factors on symptom development as persistence. Once the musculoskeletal origin of the symptoms is identified, a clinical examination schema that is based on the location of primary onset of symptoms (lumbosacral, coccygeal, sacroiliac, pelvic floor, groin or abdominal region) can be followed to establish a basis for managing the specific pain generator(s) and manage tissue dysfunction.

Benjamin Alcock and the pudendal canal.

Colebunders B, Matthew MK, Broerm N, Persing JA, Dellon AL
J Reconstr Microsurg. 2011 May 27. [Epub ahead of print]

The anatomy of the pudendal nerve is complex and difficult to visualize. Entrapment of the pudendal nerve is believed to occur in a canal, the pudendal canal or Alcock's canal, yet in the literature this term is used to refer to several different anatomic locations. We present a brief history of Benjamin Alcock, and we compare Alcock's original description of the pudendal canal with our findings from a cadaveric study. It is concluded that Alcock's canal for the pudendal nerve, as Alcock described it related to the pudendal artery, should be that portion of the pudendal nerve within the obturator internus fascia. This definition now permits future medical and surgical approaches to use the appropriate terminology for this anatomic location.

Transsacral s2-s4 nerve block for vaginal pain due to pudendal neuralgia.

Cok OY, Eker HE, Cok T, Akin S, Aribogan A, Arslan G
J Minim Invasive Gynecol. 2011 May-Jun;18(3):401-4.

Pudendal neuralgia is a type of neuropathic pain experienced predominantly while sitting, and causes a substantial decrease in quality of life in affected patients. Pudendal nerve block is a diagnostic and therapeutic option for pudendal neuralgia. Transsacral block at S2 through S4 results in pudendal nerve block, which is an option for successful relief of pain due to pudendal nerve injury. Herein is reported blockade of S2 through S4 using lidocaine and methylprednisolone for successful treatment of pudendal neuralgia in 2 patients with severe chronic vaginal pain. The patients, aged 44 and 58 years, respectively, were referred from the Gynecology Department to the pain clinic because of burning, stabbing, electric shock-like, unilateral pain localized to the left portion of the vagina and extending to the perineum. Their initial pain scores were 9 and 10, respectively, on a numeric rating scale. Both patients refused pudendal nerve block using classical techniques. Therefore, diagnostic transsacral S2-S4 nerve block was performed using lidocaine 1%, and was repeated using lidocaine 1% and methylprednisolone 80 mg after confirming block efficiency as demonstrated by an immediate decrease in pain scores. After 1 month, pain scores were 1 and 0, respectively, and both patients were free of pain at 6-month follow up. It is suggested that blockade of S2 through S4

using lidocaine and methylprednisolone is an effective treatment option in patients with chronic pudendal neuralgia when traditional pudendal nerve block is not applicable.

Surgical decompression of pudendal nerve by transperineal approach using a probe with a small balloon. [Article in French]

de Bisschop E, Nundlall R

J Gynecol Obstet Biol Reprod (Paris). 2011 May;40(3):225-30.

AIM OF THE STUDY: Describe and analyze the surgical decompression of pudendal nerve by transperineal approach using a probe with a small balloon. **PATIENTS AND METHOD:** Since 2009 may, 43 patients (31 females, 12 males) underwent for a pudendal nerve decompression. These patients had clinical symptoms of pudendal neuralgia. Neurophysiological tests based on differential staged sacral reflexes and on somesthetic evoked potentials and ultrasound investigations of pudendal vessels evoked a zone of compressive hyperpressure at the level of the axis infrapiriformis area-ischioanal fossa. In all of these 43 patients, injection block at the level of the infrapiriformis area appeared positive between one to nine months. Patients were known for this pathology since many years. Among these 43 patients, six had already pudendal nerve decompression, four by transgluteal approach and two by transvaginal (♀)/transischioanal (♂) approach but without clinical efficiency. In all of these 43 patients, surgical decompression was done by transperineal approach using a probe with a small balloon. **RESULTS AND CONCLUSION:** Surgical methodology, post-operation follow-up and results are reported hereby, which appear quite successful: after two days 77%, after one month 84% and after three months 89% of the subjects are symptom-free or with a significant reduction of pain.

Basic Science/Anatomy

Sensory innervation of the external genital tract of female guinea pigs and mice.

Vilimas PI, Yuan SY, Haberberger RV, Gibbins IL

J Sex Med. 2011 Apr 7. doi: 10.1111/j.1743-6109.2011.02258.x. [Epub ahead of print]

Introduction. The structural and neurochemical characterization of the sensory innervation of the external genitalia of females is poorly known. **Aims.** To immunohistochemically map the sensory innervation of external genitalia and surrounding structures of female guinea pigs and mice. **Methods.** Large-diameter sensory fibers, presumably mechanoreceptors, were identified by their immunoreactivity to neuron-specific enolase (NSE) or vesicular glutamate transporter 1 (VGLUT1). Peptidergic sensory fibers, presumably unmyelinated nociceptors, were identified by their immunoreactivity to calcitonin gene-related peptide (CGRP), substance P, or both. Multiple-labelled tissues were examined with high-resolution confocal microscopy. **Main Outcome Measures.** Microscopic identification of sensory endings, including potential

nociceptors, characteristic of the external genitalia. Results. Large complex nerve endings immunoreactive for NSE and VGluT1 were abundant in dermal papillae of the clitoris. Each large ending was accompanied by one or two fine fibers immunoreactive for CGRP but neither substance P nor VGluT1. More simple NSE-immunoreactive endings occurred within dermal papillae in non-hairy skin of the labia and anal canal but were rare in pudendal or perineal hairy skin. Fine intra-epithelial fibers immunoreactive for NSE but not CGRP were abundant in hairy skin but rare in non-hairy genital skin and the clitoris. Only fine varicose fibers immunoreactive for both CGRP and substance P occurred in connective tissue underlying the mucosal epithelium of cervix and endometrium. Conclusion. Compared with surrounding tissues, the sensory innervation of the clitoris is highly specialized. The coactivation of nociceptors containing CGRP but not substance P within each mechanoreceptor complex could be the explanation of pain disorders of the external genitalia.

Pain

Parsimonious collection of pain descriptors: Classification and calibration by pain patients.

Fernandez E, Krusz JC, Hall S

J Pain. 2011 Mar 14. [Epub ahead of print]

Single-word descriptors are commonly used to label and communicate pain in lay as well as clinical settings. Research has shown that the pool of 84 pain descriptors from the McGill Pain Questionnaire (MPQ) can be refined into a parsimonious subset of 36 descriptors that fit into 12 categories. However, the past 3 studies on this issue have been confined to college student samples. The present study investigated the classification structure and calibration of this new system of pain descriptors in 43 chronic pain patients. Employing a 3-point decision rule, a relatively unambiguous classification structure emerged with 3 descriptors for each of the 12 categories. Within and across categories, the intensities implied by these words could be meaningfully rank ordered. The intensities correlated positively and significantly with those previously derived from student samples as well as those of matching MPQ words previously rated by pain patients. This confirms the stability of the intensity ratings of pain words. Information theoretic analysis revealed transmission of 83% of the maximum (3.6 bits) potentially transmissible in a system of such configuration. This lends support to the idea that the 36 pain descriptors are parsimonious and can be used with efficiency to describe chronic pain. PERSPECTIVE: This study found that in the English language, 36 words (classified into 12 subcategories) can be efficiently used to describe pain. These words can also be reliably ordered in terms of implied pain intensity. This has implications for the qualitative and quantitative assessment of pain patients.

Transcutaneous spinal direct current stimulation inhibits nociceptive spinal pathway conduction and increases pain tolerance in humans.

Truini A, Vergari M, Biasiotta A, La Cesa S, Gabriele M, Di Stefano G, Cambieri C, Cruccu G, Inghilleri M, Priori A
Eur J Pain. 2011 May 14. [Epub ahead of print]

Despite concerted efforts from pharmacologic research into neuropathic pain, many patients fail to achieve sufficient pain relief with medication alone. For this reason, increasing interest centres on neurostimulation techniques. We assessed whether transcutaneous spinal direct current stimulation (tsDCS) modulates conduction in ascending nociceptive spinal pathways. We measured changes induced by anodal and cathodal tsDCS over the thoracic spinal cord on face- and foot-laser evoked potentials (LEPs) and foot-cold pressor test responses in 20 healthy subjects. Whereas anodal tsDCS reduced the amplitude of the N1 and N2 components of foot-LEPs ($P < 0.05$) neither anodal nor cathodal tsDCS changed LEPs evoked by face stimulation. Pain tolerance to the cold pressor test was significantly higher after anodal than after cathodal tsDCS ($P < 0.05$). Conversely, no difference was found in the pain threshold or pain ratings to the cold pressor test between the two polarity conditions. Our data suggest that anodal tsDCS over the thoracic spinal cord might impair conduction in the ascending nociceptive spinal pathways, thus modulating LEPs and increasing pain tolerance in healthy subjects.

Ketamine in pain management.

Cohen SP, Liao W, Gupta A, Plunkett A
Adv Psychosom Med. 2011;30:139-61.

Ketamine is an N-methyl-D-aspartate receptor antagonist that has been in clinical use in the USA for over 30 years. Its ability to provide profound analgesia and amnesia while maintaining spontaneous respiration makes it an ideal medication for procedure-related pain and trauma. In the chronic pain arena, its use continues to evolve. There is strong evidence to support its short-term use for neuropathic and nociceptive pain, and conflicting evidence for preemptive analgesia. Its potential ability to prevent 'windup' and, possibly, 'reboot' aberrant neurologic pathways in neuropathic and central pain states has generated intense interest. However, the long-term use of ketamine for chronic neuropathic pain is limited by its side effect profile, and is largely anecdotal. More research is needed to better ascertain its long-term efficacy and side effects, to determine the ideal candidates for sustained treatment and to develop means of exploiting the antinociceptive properties of ketamine while minimizing the adverse effects.

Cannabinoids for pain management.

Thaler A, Gupta A, Cohen SP

Adv Psychosom Med. 2011;30:125-38.

Cannabinoids have been used for thousands of years to provide relief from suffering, but only recently have they been critically evaluated in clinical trials. This review provides an in-depth examination of the evidence supporting cannabinoids in various pain states, along with an overview of potential adverse effects. In summary, there is strong evidence for a moderate analgesic effect in peripheral neuropathic and central pain conditions, and conflicting evidence for their use in nociceptive pain. For spasticity, most controlled studies demonstrate significant improvement. Adverse effects are not uncommon with cannabinoids, though most are not serious and self-limiting. In view of the limited effect size and low but not inconsequential risk of serious adverse events, cannabinoids should be employed as analgesics only when safer and more effective medication trials have failed, or as part of a multimodal treatment regimen.

Intrinsic membrane properties of spinal dorsal horn neurones modulate nociceptive information processing in vivo.

Realì C, Fossat P, Landry M, Russo RE, Nagy F

J Physiol. 2011 Jun 1;589(Pt 11):2733-43.

The dorsal horn of the spinal cord is the first site in the central nervous system where painful sensory information is processed before transmission to the brain. In vitro recordings in spinal slices established that this processing relies on both plasticity of synaptic connections and intrinsic electrical properties of dorsal horn neurones (DHNs). DHNs may generate plateau potentials, which underlie intense discharges and long-lasting after-discharges in response to a brief stimulation, and represent a putative endogenous mechanism for amplification of painful sensory inputs. Using patch-clamp recordings in the anaesthetized adult rat, we show that DHNs do generate plateau potentials in vivo, which shape their responses to natural sensory stimulation. Moreover, we give direct evidence for the involvement of these amplification properties in both short-term (windup) and long-term sensitisation associated with neuropathic pain, raising the possibility that plateau potentials could be putative therapeutic targets to control spinal component of neuropathic pain.

The role of nociceptin and dynorphin in chronic pain: Implications of neuro-glial interaction.

Mika J, Obara I, Przewlocka B

Neuropeptides. 2011 Apr 7. [Epub ahead of print]

Nociceptin-opioid peptide (NOP) receptor, also known as opioid receptor like-1 (ORL1), was identified following the cloning of the kappa-opioid peptide (KOP) receptor, and the characterization of these receptors revealed high homology. The endogenous ligand of NOP, nociceptin (NOC), which shares high homology to dynorphin (DYN), was discovered shortly thereafter, and since then, it has been the subject of several investigations. Despite the many

advances in our understanding of the involvement of NOC and DYN systems in pain, tolerance and withdrawal, the precise function of these systems has not been fully characterized. Here, we review the recent literature concerning the distribution of the NOC and DYN systems in the central nervous system and the involvement of these systems in nociceptive transmission, especially under chronic pain conditions. We discuss the use of endogenous and exogenous ligands of NOP and KOP receptors in pain perception, as well as the potential utility of NOP ligands in clinical practice for pain management. We also discuss the modulation of opioid effects by NOC and DYN. We emphasize the important role of neuro-glial interactions in the effects of NOC and DYN, focusing on their presence in neuronal and non-neuronal cells and the changes associated with chronic pain conditions. We also present the dynamics of immune and glial regulation of neuronal functions and the importance of this regulation in the roles of NOC and DYN under conditions of neuropathic pain and in the use of drugs that alter these systems for better control of neuropathic pain.

The dynamic TRPA1 channel: A suitable pharmacological pain target?

Garrison SL, Stucky CL

Curr Pharm Biotechnol. 2011 Apr 5. [Epub ahead of print]

Acute pain detection is vital to navigate and survive in one's environment. Protection and preservation occur because primary afferent nociceptors transduce adverse environmental stimuli into electrical impulses that are transmitted to and interpreted within high levels of the central nervous system. Therefore, it is critical that the molecular mechanisms that convert noxious information into neural signals be identified and their specific functional roles delineated in both acute and chronic pain settings. The Transient Receptor Potential (TRP) channel family member TRP ankyrin 1 (TRPA1) is an excellent candidate molecule to explore and intricately understand how single channel properties can tailor behavioral nociceptive responses. TRPA1 appears to dynamically respond to an amazingly wide range of diverse stimuli that include apparently unrelated modalities such as mechanical, chemical and thermal stimuli that activate somatosensory neurons. How such dissimilar stimuli activate TRPA1, yet result in modality-specific signals to the CNS is unclear. Furthermore, TRPA1 is also involved in persistent to chronic painful states such as inflammation, neuropathic pain, diabetes, fibromyalgia, bronchitis and emphysema. Yet how TRPA1's role changes from an acute sensor of physical stimuli to its contribution to these diseases that are concomitant with implacable, chronic pain is unknown. TRPA1's involvement in the nociceptive machinery that relays the adverse stimuli during painful disease states is of considerable interest for drug delivery and design by many pharmaceutical entities. In this review, we will assess the current knowledge base of TRPA1 in acute nociception and persistent inflammatory pain states, and explore its potential as a therapeutic pharmacological target in chronic pervasive conditions such neuropathic pain, persistent inflammation and diabetes.

Pain perception during menstrual cycle.

de Tommaso M

Curr Pain Headache Rep. 2011 May 10. [Epub ahead of print]

Sexual hormones influence complex brain function and pain perception. Many psychophysical studies attempted to establish pain perception changes across menstrual cycle in animal models and healthy women or those with chronic pain. General results are quite uncertain in regard to consistent menstrual-related fluctuations of pain perception. The few studies applying neurophysiological procedures to test pain-related changes during menstrual cycle suggested a fluctuation of central modulation of pain across phases, with a prevalence of excitatory versus inhibitory control in the premenstrual period, which may explain the cyclic worsening of many syndromes, such as migraine. Whatever is the relevance of menstrual cycle on individual painful symptoms, it should be accepted as one of the numerous factors influencing mechanisms of neuromodulation.

Systematic review of the comparative effectiveness of antiepileptic drugs for fibromyalgia.

Siler AC, Gardner H, Yanit K, Cushman T, McDonagh M

J Pain. 2011 Apr;12(4):407-15.

Fibromyalgia is a difficult-to-treat chronic pain syndrome that affects 2% of the US population. Pregabalin is an antiepileptic recently FDA approved for fibromyalgia treatment. Other antiepileptics have been suggested for treatment. This systematic review examines the relative benefits and harms of antiepileptic drugs in the treatment of fibromyalgia. A literature search was conducted and 8 studies matched criteria (7 studies of pregabalin, 1 of gabapentin). Both drugs reduced mean pain scores more than placebo at a modest rate (pregabalin, 38% to 50%; gabapentin, 51%). In a 6-month trial of pregabalin responders, 32% continued to have response at 6 months, with a mean time to loss of response of 34 days. Compared to placebo, the drugs had similarly high rates of adverse events and withdrawals. Without a head-to-head trial it is not possible to conclude if 1 antiepileptic is more effective or harmful than the other, although limited evidence suggests potential differences. Future studies must directly compare the drugs, include a more broadly defined population, examine long term benefits and harms, and include co-interventions. We conclude that pregabalin and gabapentin are modestly effective for the treatment of fibromyalgia but that their long-term safety and efficacy remain unknown.

Other Vulvovaginal Disorders

Erythema and burning pain in the vulva: a possible phenotype of erythromelalgia.

Johnson E, Iyer P, Eanes A, Zolnoun D.

Case Reports in Medicine. Volume 2011, Article ID 374167, doi:10.1155/2011/374167

Free online text: <http://www.hindawi.com/journals/crim/2011/374167/>

We report a case of burning vulvar pain accompanied by erythema responding to an oral combination of a benzodiazepine and a beta blocker. The positive response to two medication classes used in the treatment of erythromelalgia supports the possibility of a localized manifestation of this disorder in the genital region.

Alternative therapies in women with chronic vaginitis.

Nyirjesy P, Robinson J, Mathew L, Lev-Sagie A, Reyes I, Culhane JF
Obstet Gynecol. 2011 Apr;117(4):856-61.

OBJECTIVES: To describe the use of complementary alternative medicines in women with chronic vaginitis and to evaluate epidemiologic factors associated with these treatments. **METHODS:** In this prospective cohort study, patients with chronic vaginitis completed a questionnaire about past diagnoses and treatments. Information regarding demographics, medical and social history, perceived mental and emotional stress, and current symptoms was collected. All patients underwent a standard physical examination and laboratory testing and were assigned a specific diagnosis. **RESULTS:** A total of 481 women were enrolled; 64.9% used complementary alternative medicines. The most common treatments were yogurt and acidophilus pills. In univariate analysis, compared with nonusers, users of complementary alternative medicines were younger (83.4% younger than 50 compared with 73.1%; $P=.032$), not African American (11.9% compared with 21.3%; $P=.018$), had increased measures of perceived stress ($P=.008$), and reported that their symptoms interfered with both work (59.1% compared with 40.6%; $P=.001$) and social lives (57.9% compared with 40.2%; $P=.001$). Patients using complementary alternative medicines had seen more doctors (median 2 compared with 1; $P<.001$) and were more likely to report a history of vulvovaginal candidiasis (98.4% compared with 90.5%; $P<.001$) or bacterial vaginosis (34.3% compared with 22.8%; $P=.007$). In the multivariable analysis, interference with social life, higher number of doctors seen, symptoms of itching or burning, and previous diagnoses of yeast infection remained associated with alternative medicine use. A current diagnosis of vulvovaginal candidiasis was not associated with alternative medicine use. **CONCLUSION:** Complementary alternative medicine use is common in women with chronic vaginitis, particularly in those who are young, have more disruptive symptoms, and report greater stress.

Treating menopausal symptoms with a tissue-selective estrogen complex.

Levine JP
Gend Med. 2011 Apr;8(2):57-68.

Vasomotor symptoms and vulvar-vaginal atrophy are common consequences of menopause, and the only treatment approved by the US Food and Drug Administration is hormone therapy. Because both physicians and women are concerned with the tolerability and safety profile of estrogen and estrogen plus progestin treatments, alternative menopause therapies are needed. An ideal menopause treatment modality would relieve menopausal vasomotor and vulvar-

vaginal symptoms, maintain bone mass, and have neutral or beneficial cardiovascular effects, without stimulating the breast or endometrium. The novel tissue-selective estrogen complex (TSEC) agent was paired with a selective estrogen receptor modulator (SERM) with estrogen(s) in an attempt to achieve a more favorable clinical profile based on the blended tissue activities of its components. This article reviews the published reports from Phase III trials of TSEC, which paired bazedoxifene (BZA) and conjugated estrogens (CEs). BZA/CE alleviated menopausal symptoms and prevented postmenopausal bone loss, had an overall good safety profile with an incidence of amenorrhea and breast pain similar to that with placebo, and did not stimulate the endometrium. The largest (N = 3397) and longest (2 years) study of this TSEC containing BZA/CE demonstrated endometrial hyperplasia rates similar to that with placebo and changes in lumbar spine bone mineral density that were significantly better than that with placebo, when a minimum dose of 20 mg of BZA was used with 0.625 or 0.45 mg of CE. Subsequent smaller studies showed that BZA/CE effectively reduced the incidence and frequency of hot flushes and significantly improved signs and symptoms of vaginal atrophy. Longer term safety with regard to cardiovascular and breast effects have not been established. Given the efficacy and safety reported in these Phase III trials, the TSEC of BZA/CE may be a promising new option for the treatment of menopause.

Carcinosarcoma ex eccrine spiradenoma of the vulva: report of the first case.

Chen G, Cheuk W, Cheung JS, Chan JK.

Int J Gynecol Pathol. 2011 May;30(3):301-5.

Carcinosarcoma is exceedingly rare in the vulva. We describe a case of carcinosarcoma in a 67-year-old female patient who presented with recent enlargement and pain of a vulval nodule noted for 15 years. The excised tumor showed intermixed carcinomatous (adenocarcinoma and anaplastic carcinoma) and sarcomatous elements (osteosarcoma, chondrosarcoma, and leiomyosarcoma), which focally merged with several lobules of typical eccrine spiradenoma. The inguinal lymph nodes showed metastasis of the carcinomatous component only. This case represents the first reported case of vulval carcinosarcoma of the skin adnexal origin, and has to be distinguished from sarcomatoid carcinoma of epidermal origin because of a probable more aggressive behavior.

Superficial granulomatous pyoderma of the vulva in a patient receiving maintenance rituximab (MabThera) for lymphoma.

Walsh M, Leonard N, Bell H.

J Low Genit Tract Dis. 2011 Apr;15(2):158-60.

BACKGROUND: Vulval ulceration can be caused by a wide variety of etiological factors including bacterial and viral infections, granulomatous disorders, and malignancy. Superficial granulomatous pyoderma (SGP) is a variant of pyoderma gangrenosum. It is characterized by localized ulcerative lesions that may be precipitated by surgery. We report a case of vulval SPG in an immunocompromised patient. **CASE:** A 51-year-old woman presented with a 6-week

history of severe vulval pain, bleeding, and rapidly progressing ulceration. She had a previous history of relapsed follicular non-Hodgkin lymphoma and was currently receiving regular MabThera (Welwyn Garden City, Hertfordshire, UK). Examination revealed deep ulceration involving the entire vulva and extending into the vagina with areas of necrosis. Histological examination showed ulceration with sparse granulomas and eosinophils. The clinical and histological findings confirmed a diagnosis of SGP. CONCLUSIONS: Vulval ulceration in an immunocompromised patient has a broad differential diagnosis. The possibility of a granulomatous condition such as SGP must always be considered.

Management of lichen sclerosus with triamcinolone ointment: Effectiveness in reduction of patient symptom scores.

Lefevre C, Hoffstetter S, Meyer S, Gavard J

J Low Genit Tract Dis. 2011 May 7. [Epub ahead of print]

OBJECTIVE: To determine whether topical triamcinolone ointment effectively reduces patient's symptoms for the management of lichen sclerosus (LS). MATERIALS AND METHODS: A retrospective chart review of LS patients seen during 2004 to 2008 in the Saint Louis University Vulvar Clinic was conducted. Inclusion criteria were biopsy-confirmed LS and age 18 years and older. Data were collected at the initial visit and at 6 to 10 weeks, 3 months, and 6 months of follow-up. Effectiveness was assessed using symptom scores on a Likert scale. Data were analyzed using either paired t tests or nonparametric Wilcoxon signed rank tests using a p value less than .05 to denote statistical significance. RESULTS: Of 41 women, 34 met inclusion criteria. Vulvar pruritus was the most frequently reported vulvar symptom, occurring in 32 (94.1%) of 34 women. Dyspareunia, vulvar burning, and vulvar pain were reported in 17 (54.8%) of 31, 22 (64.7%) of 34, and in 13 (38.2%) of 34 women, respectively. Statistically significant reductions in mean symptom scores between the initial and the 6- to 10-week follow-up visits were found for dyspareunia, vulvar burning, vulvar pruritus, and pain (p values <.05 to <.001) and at 3-month follow-up visits for dyspareunia, vulvar burning, and vulvar pruritus (p <.05). Complete symptom relief was reported for 8 (47.1%) of 17 women with dyspareunia, 19 (86.4%) of 22 women with vulvar burning, 23 (71.9%) of 32 women with vulvar pruritus, and 12 (92.3%) of 13 women with vulvar pain. CONCLUSIONS/IMPLICATIONS FOR PRACTICE: Topical triamcinolone ointment is an effective treatment for the management of LS based on the significant reduction of patient symptom scores. Inherent risks with long-term use of high-potency corticosteroids should prompt all practitioners to consider triamcinolone ointment as a safer long-term treatment for patients with LS.

Treatment of recurrent vulvovaginal candidiasis.

Davis JD, Harper AL

Am Fam Physician. 2011 Jun 15;83(12):1482-4.

No abstract available.

Antifungal efficacy of propolis against fluconazole-resistant *Candida glabrata* isolates obtained from women with recurrent vulvovaginal candidiasis.

Shokri H, Khosravi AR, Yalfani R

Int J Gynaecol Obstet. 2011 Jun 11. [Epub ahead of print]

No abstract available.

Association between mannose-binding lectin and interleukin-1 receptor antagonist gene polymorphisms and recurrent vulvovaginal candidiasis.

Wojitani MD, de Aguiar LM, Baracat EC, Linhares IM

Arch Gynecol Obstet. 2011 Jun 8. [Epub ahead of print]

OBJECTIVE: The influence of functional polymorphisms in the genes coding for mannose-binding lectin (MBL) and interleukin-1 receptor antagonist (IL-1ra) on recurrent vulvovaginal candidiasis (RVVC) were examined in an urban Brazilian population. **METHODS:** DNA was isolated from buccal swabs of 100 women with RVVC and 100 control women and tested by gene amplification for a single nucleotide polymorphism in codon 54 of the MBL2 gene and for a length polymorphism in intron 2 of the IL1RN gene. Genotype and allele frequencies were compared between groups. **RESULTS:** The frequency of the variant MBL2 B allele, associated with reduced circulating and vaginal MBL concentrations, was 27.0% in RVVC and 8.5% in control women ($p < .0001$). The MBL2 B,B genotype was present in 12% of RVVC patients and 1% of controls ($p = .0025$). The IL1RN 2 allele frequency, associated with the highest level of unopposed IL-1 β activity, was 24.0% in RVVC and 23.4% in controls. The IL1RN genotype distribution was also similar in both groups. **CONCLUSION:** Carriage of the MBL2 codon 54 polymorphism, but not the IL1RN length polymorphism, predisposes to RVVC in Brazilian women.

Claudin and p53 expression in vulvar lichen sclerosus and squamous-cell carcinoma.

Sadalla JC, Lourenço SV, Sotto MN, Baracat EC, Carvalho JP

J Clin Pathol. 2011 Jun 4. [Epub ahead of print]

Aims. Vulvar squamous-cell carcinoma (SCC) is a rare gynaecological cancer. Vulvar SCC has been shown to develop from vulvar intraepithelial neoplasias, which are related to lichen sclerosus (LS). Most studies to date have compared vulvar SCC with LS only morphologically, but no detailed molecular analysis has been performed. The objective was to compare claudin and p53 expression in these diseases and determine if there was any association with expression and vulvar SCC progression. **Methods** Immunohistochemical analysis was performed in order to determine expression of p53 and claudin 1, 2, 3, 4, 5, 7 and 11 in human vulvar tissue samples from LS, SCC and control patients. **Results** Claudin 1, 2, 3, 4 and 5 were expressed comparably in the three groups. Claudin 7 and 11 expression was significantly decreased in LS and SCC samples compared with the control group. Expression of p53 was significantly increased in SCC

and LS patient samples compared with the control group. Claudin 7 and 11 were not expressed in LS and SCC. However, there was no significant difference in expression of any of the claudins between the LS and SCC samples. Furthermore, p53 expression is the highest in SCC patients and lowest in the control group. However, expression of p53 did not vary between samples from isolated LS and LS associated SCC patients, suggesting that increased p53 expression is not the determining factor in the progression of LS lesions to SCC.

Modulation of morphogenesis in *Candida albicans* by various small molecules.

Shareck J, Belhumeur P

Eukaryot Cell. 2011 Jun 3. [Epub ahead of print]

The pathogenic yeast *Candida albicans*, a member of the mucosal microbiota, is responsible for a large spectrum of infections, ranging from benign thrush and vulvovaginitis in both healthy and immunocompromised individuals to severe, life-threatening infections in immunocompromised patients. A striking feature of *C. albicans* is its ability to grow as budding yeast and as filamentous forms, including hyphae and pseudohyphae. The yeast-to-hypha transition contributes to the overall virulence of *C. albicans* and may even constitute a target for the development of antifungal drugs. Indeed, impairing morphogenesis in *C. albicans* has been shown to be a means to treat candidiasis. Additionally, a large number of small molecules such as farnesol, fatty acids, rapamycin, geldanamycin, histone deacetylase inhibitors, and cell cycle inhibitors have been reported to modulate the yeast-to-hypha transition in *C. albicans*. In this review, we take a look at molecules that modulate morphogenesis in the pathogenic yeast. When possible, we address experimental findings regarding their mechanisms of action and their therapeutic potential. We discuss whether or not modulating morphogenesis constitutes a strategy to treat *Candida* infections.

Vaginitis: diagnosis and treatment.

Hainer BL, Gibson MV

Am Fam Physician. 2011 Apr 1;83(7):807-15.

Bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis are the most common infectious causes of vaginitis. Bacterial vaginosis occurs when the normal lactobacilli of the vagina are replaced by mostly anaerobic bacteria. Diagnosis is commonly made using the Amsel criteria, which include vaginal pH greater than 4.5, positive whiff test, milky discharge, and the presence of clue cells on microscopic examination of vaginal fluid. Oral and topical clindamycin and metronidazole are equally effective at eradicating bacterial vaginosis. Symptoms and signs of trichomoniasis are not specific; diagnosis by microscopy is more reliable. Features of trichomoniasis are trichomonads seen microscopically in saline, more leukocytes than epithelial cells, positive whiff test, and vaginal pH greater than 5.4. Any nitroimidazole drug (e.g., metronidazole) given orally as a single dose or over a longer period resolves 90 percent of trichomoniasis cases. Sex partners should be treated simultaneously. Most patients with vulvovaginal candidiasis are diagnosed by the presence of vulvar inflammation plus vaginal

discharge or with microscopic examination of vaginal secretions in 10 percent potassium hydroxide solution. Vaginal pH is usually normal (4.0 to 4.5). Vulvovaginal candidiasis should be treated with one of many topical or oral antifungals, which appear to be equally effective. Rapid point-of-care tests are available to aid in accurate diagnosis of infectious vaginitis. Atrophic vaginitis, a form of vaginitis caused by estrogen deficiency, produces symptoms of vaginal dryness, itching, irritation, discharge, and dyspareunia. Both systemic and topical estrogen treatments are effective. Allergic and irritant contact forms of vaginitis can also occur.

Vulvar verruciform xanthoma: Ten cases associated with lichen sclerosus, lichen planus, or other conditions.

Fite C, Plantier F, Dupin N, Avril MF, Moyal-Barracco M
Arch Dermatol. 2011 May 16. [Epub ahead of print]

BACKGROUND: Verruciform xanthoma (VX) is a rare benign tumor that usually involves the oral cavity. Since the first report of this tumor in 1971, only 9 cases have been reported on the vulva, and 3 of these were associated with another vulvar condition. We describe the clinicopathologic features of 10 patients with vulvar VX and focus on their associated conditions. **Observation:** The mean age of the patients was 68 years (range, 51-80 years). The VX lesions were asymptomatic, yellowish-orange verrucous plaques. The diagnosis was clinically suspected in 2 cases; other suggested diagnoses were condyloma or squamous cell carcinoma. All of the patients had an associated vulvar condition: lichen sclerosus (6 patients), lichen planus (2 patients), Paget disease, or radiodermatitis. Under microscopy, the VX lesions displayed parakeratosis, acanthosis without atypia, and elongated rete ridges. Xanthomatous cells were aggregated in the papillary dermis. **CONCLUSIONS:** Vulvar VX is a benign tumor with misleading clinical features. All 10 cases were associated with a vulvar condition, mainly a lichen sclerosus. Therefore, VX might represent a reaction pattern induced by different conditions, mainly characterized by damage to the dermoepidermal junction. When confronted with the diagnosis of vulvar VX, clinicians may look for an associated vulvar condition.

In vivo activity of Sapindus saponaria against azole-susceptible and -resistant human vaginal Candida species.

Damke E, Tsuzuki JK, Cortez DA, Ferreira IC, Bertoni TA, Batista MR, Donati L, Svidzinski Tle, Consolaro ME
BMC Complement Altern Med. 2011 May 4;11:35.

BACKGROUND: Study of in vivo antifungal activity of the hydroalcoholic extract (HE) and n-BuOH extract (BUTE) of *Sapindus saponaria* against azole-susceptible and -resistant human vaginal *Candida* spp. **METHODS:** The in vitro antifungal activity of HE, BUTE, fluconazole (FLU), and itraconazole (ITRA) was determined by the broth microdilution method. We obtained values of minimal inhibitory concentration (MIC) and minimum fungicide concentration (MFC) for 46 strains of *C. albicans* and 10 of *C. glabrata* isolated from patients with vulvovaginal candidiasis (VVC). VVC was induced in hyperestrogenic Wistar rats with azole-susceptible *C.*

albicans (SCA), azole-resistant *C. albicans* (RCA), and azole-resistant *C. glabrata* (RCG). The rats were treated intravaginally with 0.1 mL of HE or BUTE at concentrations of 1%, 2.5% and 5%; 100 µg/mL of FLU (treatment positive control); or distilled water (negative control) at 1, 24, and 48 h after induction of the infection, and the progress of VVC was monitored by culturing and scanning electron microscopy (SEM). The toxicity was evaluated in cervical cells of the HeLa cell line. RESULTS: The extracts showed in vitro inhibitory and fungicidal activity against all the isolates, and the MIC and MFC values for the *C. glabrata* isolates were slightly higher. In vivo, the SCA, RCA, and RCG infections were eliminated by 21 days post-infection, with up to 5% HE and BUTE, comparable to the activity of FLU. No cytotoxic action was observed for either extract. CONCLUSIONS: Our results demonstrated that HE and BUTE from *S. saponaria* show inhibitory and fungicidal activity in vitro, in addition to in vivo activity against azole-resistant vaginal isolates of *C. glabrata* and azole-susceptible and resistant isolates of *C. albicans*. Also considering the lack of cytotoxicity and the low concentrations of the extracts necessary to eliminate the infection in vivo, HE and BUTE show promise for continued studies with purified antifungal substances in VVC yeast isolates.

The impact of the latest classification system of benign vulvar diseases on the management of women with chronic vulvar pruritus.

Kelekci KH, Adamhasan F, Gencdal S, Sayar H, Kelekci S
Indian J Dermatol Venereol Leprol. 2011 May-Jun;77(3):294-9.

BACKGROUND: The management of women with chronic benign vulvar dermatoses has been one of the most difficult and challenging aspects of women's healthcare for a long time. AIM: Our aim was to compare the ability to approach the specific diagnosis of nonneoplastic and noninfectious vulva diseases, between the new classification system and the old classification system. METHODS: One hundred women with chronic vulvar pruritus were included in the study. After detailed examination of the vulva, all visible lesions were biopsied, with normal skin included. All specimens were sent for dermatopathology and examined simultaneously under a binocular microscope by two pathologists. Specific diagnosis if possible and histopathological findings were classified according to both the 1987 and 2006 International Society for the Study of Vulvar Diseases (ISSVD) classifications. The ratios that were able to be approached on the specific diagnosis, with the aid of the two classification systems, were compared. RESULTS: Specific clinical diagnosis by both pathological and after using clinicopathological correlation was possible in 69 out of 91 patients (75.8%) according to the 1987 ISSVD classification, and in 81 out of 91 patients (89.0%) according to the ISSVD 2006 classification system. The difference in the clinical diagnosis ratios between the two classification systems was statistically significant ($P < 0.05$). In a subgroup of women without specific diagnosis at the time of pathological examination, clinical diagnosis was made in 28 out of 50 women (56%) after using the clinicopathological correlation according to the ISSVD 1987 classification, whereas, specific diagnosis was made in 39 out of 49 (79.6%) women after using the clinicopathological correlation according to the ISSVD 2006 classification. The difference was statistically significant in terms of the ratio of the ability to achieve a specific diagnosis ($P < 0.01$). CONCLUSION: ISSVD 2006 classification of nonneoplastic and noninfectious vulvar

disease is more useful than the former classification, in terms of approaching the specific diagnosis of vulvar dermatoses.