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Feature Article

Urogenital symptoms and pain history as precursors of vulvodynia: a longitudinal study.

Reed BD, Payne CM, Harlow SD, Legocki LJ, Haefner HK, Sen A

J Womens Health (Larchmt). 2012 Nov;21(11):1139-43. doi: 10.1089/jwh.2012.3566.

BACKGROUND: We sought to assess vulvodynia incidence and risk factors among those with and without premorbid urogenital symptoms. METHODS: Women's Health Registry members who completed a baseline assessment in 2004 were sent a 2-year and 4-year follow-up survey containing a validated screen for vulvodynia. Subgroup analysis of vulvodynia incidence rates was performed, and risk factors associated with incidence were assessed. RESULTS: Of 1037 original enrollees, 723 (69.7%) completed consecutive surveys (initial and 2-year or initial, 2-year, and 4-year), 660 of whom did not have current or past vulvodynia at baseline. Of these 660, 71 (10.8%) first met criteria for vulvodynia within the 4-year period, for an annual incidence rate of 3.1% (95% confidence interval [CI] 2.5-4.0). Baseline strict controls were less likely to develop criteria for vulvodynia diagnosis (annual incidence rate of 1.4%) compared to those with an intermediate phenotype (presence of dyspareunia or history of short-term vulvar pain), for whom the incidence rate was 5.6% ($p<0.001$). Risk factors for incident vulvodynia differed between these two groups. Among the strict controls, an increased risk was noted among younger women (incidence rate ratio) [IRR] 3.6). For those with an intermediate phenotype, risk was increased among nonwhite women and those reporting pain with or after intercourse (IRR 2.2, 3.4, and 3.1, respectively). In both control groups, incident vulvodynia risk increased among those reporting urinary burning at enrollment (IRR 4.2 and 2.8 for strict and intermediate phenotype controls, respectively). CONCLUSIONS: The annual incidence of vulvodynia is substantial (3.1%) and is greater among women reporting a history of dyspareunia or vulvar pain that did not meet criteria for vulvodynia compared to those without this history, suggesting that generalized urogenital sensitivity may be a common underlying mechanism predating the clinical presentation of vulvodynia.

Vulvodynia /Vulvovaginal Pain

With the identification of a high-risk group for the development of vulvodynia comes an eye on prevention.

Nguyen RH

J Womens Health (Larchmt). 2012 Nov;21(11):1130-1. doi: 10.1089/jwh.2012.3967.

An article in this issue [Reed et. al. above] of the Journal brings the field one important step closer to improved description of the natural progression, specifically from a nondisease state to vulvodynia. A high-risk group of women

for the development of diagnosable vulvodynia is women showing some component of vulvodynia, such as pain with first tampon insertion or intercourse and vulvar burning. Even within this high-risk group, however, additional factors may increase the risk of vulvodynia diagnosis, and these factors include nonwhite race, pain after intercourse, and burning with urination. Priorities for vulvodynia research can now evolve into theories for primary or secondary prevention of this consuming condition.

Effect of lubricating gel on patient comfort during vaginal speculum examination: a randomized controlled trial.
Hill DA, Lamvu G
Obstet Gynecol. 2012 Feb;119(2 Pt 1):227-31.

OBJECTIVE: To estimate the efficacy of lubricating gel compared with using water for pain during vaginal speculum insertion. METHODS: This study was a randomized trial of nonpregnant women aged 18-50 years who required a vaginal speculum examination between February and July 2011. Patients blinded to study assignment underwent vaginal speculum examination using a standardized technique with a medium-sized plastic speculum prepared with either 0.3 mL lubricating gel or 3 mL of water used to cover both speculum blades. Patients recorded pain using a 10-cm visual analog scale immediately after speculum insertion. A pre hoc power analysis determined that 55 patients in each arm would be required to detect a difference of 0.9 cm on a 10-cm visual analog scale. RESULTS: A total of 299 consecutive women requiring vaginal speculum examination were screened for enrollment and 120 women were randomized with 60 per group. There were no marked differences in the demographic characteristics of the gel (n=59) and water (n=60) participants available for final analysis. The gel group showed significantly lower pain scores for speculum insertion (mean ± standard deviation: 1.41±1.55 compared with water 2.15±1.93, P<.01). Of patients undergoing examination with gel, 20 of 59 (33.9%) marked zero on the pain scale compared with six of 60 (10%) patients receiving water (P=.002). All 73 patients who underwent Pap screening had adequate cytology. CONCLUSION: Applying a small amount of lubricating gel significantly decreases patient pain during vaginal speculum insertion.

Clinical and therapeutic aspects of vulvodynia: the importance of physical therapy.
Polpeta NC, Giraldo PC, Teatin Juliato CR, Gomes Do Amaral RL, Moreno Linhares I, Romero Leal Passos M
Minerva Ginecol. 2012 Oct;64(5):437-45.

Vulvodynia affects a large number of women worldwide. It is estimated that the prevalence rate of vulvodynia is 16% in women aged 18 to 64 years, resulting in constant demand for specialized medical care, although little therapeutic success is achieved. Furthermore, the cause of this disorder remains unknown and involves different symptoms that are implicated in important chronic vulvar pain with disastrous consequences for the afflicted women. In view of these data, the authors have proposed a bibliographic review of the pathophysiology and treatment of vulvodynia. The aim of this review was to assist in clinical diagnosis and elucidate the multidisciplinary treatment that appears to be associated with a higher success rate in these women. Physical therapy using diverse techniques has an important role in multidisciplinary care, obtaining satisfactory results in the treatment of pelvic floor muscle dysfunction and thus improving the symptoms and quality of life in women with vulvodynia.

Health-related quality of life in patients with interstitial cystitis/bladder pain syndrome and frequently associated comorbidities.
Suskind AM, Berry SH, Suttorp MJ, Elliott MN, Hays RD, Ewing BA, Clemens JQ
Qual Life Res. 2012 Oct 7. [Epub ahead of print]

PURPOSE: To estimate the association of chronic non-urologic conditions [i.e., fibromyalgia (FM), chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS)] with health-related quality of life (HRQOL) in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). METHODS: A total of 276 women with established diagnoses of IC/BPS completed a telephone interview which included demographics, self-reported medical conditions, the SF-36

health survey, and the interstitial cystitis symptom index (ICSI). Of the 276 study participants, 82 (30%) had IC/BPS plus another pelvic pain condition (overactive bladder, endometriosis, or vulvodynia). Multivariate linear regression analysis was used to identify correlates of SF-36 physical and mental component summary scores. RESULTS: Mean patient age was 45.1 (SD 15.9) years, and 83 % of the subjects were white. Mean values for the SF-36 Physical Component Score (PCS) and Mental Component Score (MCS) means were 39 (SD 14) and 45 (SD 12), respectively, indicating significant HRQOL reductions. Mean ICSI score was 11.27 (SD = 4.86). FM and IBS were significantly associated with worse SF-36 scores: -8 points on the PCS ($p < 0.001$) and -6 points on the MCS ($p < 0.001$). CFS and the presence of other pelvic conditions (overactive bladder, vulvodynia, endometriosis) were not significantly associated with SF-36 PCS and MCS scores. CONCLUSIONS: In patients with IC/BPS, the presence of FM, CFS, and IBS has a significant association with HRQOL, equivalent in impact to the bladder symptoms themselves. These results emphasize the importance of a multidisciplinary approach to treating patients with IC/BPS and other conditions.

Vulvodynia and interstitial cystitis: Causes of pelvic pain.
Hoffstetter, S
Medscape Medical News, Steven Fox Oct 30, 2012

A presentation at the National Association of Nurse Practitioners in Women's Health (NPWH) 15th Annual Conference, held in Orlando, Florida, highlighted insights on vulvodynia and interstitial cystitis, and provided practical tips on how to diagnosis and manage patients with those conditions. In an email interview with Medscape Medical News, Susan Hoffstetter, PhD, WHNP-BC, FAANP, associate professor in the Department of Obstetrics, Gynecology, and Women's Health at the Saint Louis University School of Medicine in Missouri, discussed her presentation.

Urogynecological causes of pain and the effect of pain on sexual function in women.
Dhingra C, Kellogg-Spadt S, McKinney TB, Whitmore KE
Female Pelvic Med Reconstr Surg. 2012 Sep-Oct;18(5):259-67.

Female Sexual Dysfunction (FSD) is a complex biopsychosocial phenomenon. Screening, identifying and managing urogenital and sexual symptoms often result in significant improvement in women's quality of life. Providers must proactively question patients about possible presence of FSD. When a sexual problem is present, identify the type of FSD, counsel patients on the appropriate approaches to treatment. No single therapeutic approach is effective in treating all types of FSD.

Efficacy of psychosocial interventions in men and women with sexual dysfunctions-A systematic review of controlled clinical trials: Part 2-The efficacy of psychosocial interventions for Female Sexual Dysfunction.
Günzler C, Berner MM
J Sex Med. 2012 Oct 22. doi: 10.1111/j.1743-6109.2012.02965.x. [Epub ahead of print]

INTRODUCTION: As yet, a summary of the research evidence concerning the efficacy of psychological treatment in female sexual dysfunction is lacking. Previous reviews were often nonsystematic or explored one specific sexual dysfunction. AIM: Our systematic review provides an overview of the efficacy of psychosocial interventions in all female sexual dysfunction. MAIN OUTCOME MEASURES: Main outcome measures included for example psychometrically validated scales, diary notes, interviews, and vulvar algesiometer. The efficacy of psychosocial interventions was measured for example by the frequency of and satisfaction with sexual activity and sexual functioning. Safety and acceptance were evaluated on the basis of adverse events and dropout rates. METHODS: The systematic literature search included electronic database search, handsearch, contact with experts, and an ancestry approach. Studies were included if the woman was given a formal diagnosis of a sexual dysfunction (International Statistical Classification of Diseases and Related Health Problems-ICD10/-9; Diagnostic and Statistical Manual of Mental Disorders-IV/-III-R) and when the intervention was psychosocial or psychotherapeutic. The control group included either another treatment or a

waiting-list control group. The report of relevant outcomes was necessary for inclusion as well as the design of the study (randomized, controlled trials [RCTs] and controlled clinical trials). The assessment of methodological quality comprised aspects of randomization, blinding, incomplete outcome data, selective reporting, and allegiance. RESULTS: We identified 15 RCTs that investigated efficacy in female sexual dysfunction and two further studies that examined male and female sexual dysfunction together. Most trials explored sexual pain disorders. About half of all studies in women used either a concept derived from Masters and Johnson or a cognitive-behavioral treatment program. Both approaches showed significant improvements compared with a control group. Benefit was not always maintained over the (variable) follow-up period. CONCLUSIONS: Traditional sexual therapeutic concepts proved to be efficacious in the treatment of female sexual dysfunction. A shortcoming was the rather low methodological quality of included studies.

The Sexual Disgust Questionnaire; a psychometric study and a first exploration in patients with sexual dysfunctions.
van Overveld M, de Jong PJ, Peters ML, van Lankveld J, Melles R, Ter Kuile MM
J Sex Med. 2012 Oct 22. doi: 10.1111/j.1743-6109.2012.02979.x. [Epub ahead of print]

INTRODUCTION: Disgust may be involved in sexual problems by disrupting sexual arousal and motivating avoidance of sexual intercourse. To test whether heightened disgust for sexual contaminants is related to sexual dysfunctions, the Sexual Disgust Questionnaire (SDQ) has recently been developed. Previous research showed that particularly women with vaginismus display a generally heightened dispositional disgust propensity and heightened disgust toward stimuli depicting sexual intercourse. AIM: To determine the psychometric properties of the SDQ and test whether heightened disgust toward sexual stimuli is specific to vaginismus or can be observed in other sexual dysfunctions as well. Methods. First, a large sample of undergraduates and university employees completed the SDQ (N = 762) and several trait disgust indices. Next, women with vaginismus (N = 39), dyspareunia (N = 45), and men with erectile disorder (N = 28) completed the SDQ and were compared to participants without sexual problems (N = 70). MAIN OUTCOME MEASURE: SDQ to index sexual disgust. RESULTS: The SDQ proved a valid and reliable index to establish disgust propensity for sexual stimuli. Supporting construct validity of the SDQ, sexual disgust correlated with established trait indices. Furthermore, sexual disgust and willingness to handle sexually contaminated stimuli were associated with sexual functioning in women, but not in men. Specifically women with vaginismus displayed heightened sexual disgust compared to women without sexual problems, while men with erectile disorders demonstrated a lower willingness to handle sexually contaminated stimuli compared to men without sexual problems. CONCLUSIONS: The SDQ appears a valid and reliable measure of sexual disgust. The pattern of SDQ-scores across males and females with and without sexual dysfunctions corroborates earlier research suggesting that disgust appraisals are involved especially in vaginismus and supports the view that the difficulty with vaginal penetration experienced by women in vaginismus may partly be due to disgust-induced defensive reflexes that could disrupt sexual arousal.

Hormonal contraceptives and women's sexuality: A comment on Burrows et al.
Graham CA, Bancroft J
J Sex Med. 2012 Oct 11: DOI: 10.1111/j.1743-6109.2012.02957.x

No Abstract Available.

Surgical location and anatomical variations of pudendal nerve.
Matejčík V
ANZ J Surg. 2012 Sep 19. doi: 10.1111/j.1445-2197.2012.06272.x. [Epub ahead of print]

BACKGROUND: An objective of our work was to clarify variations in pudendal nerve formation, as well as their possible impact on the clinical picture. METHOD: Bilateral pudendal nerve course and formation was studied on 20 adult cadavers. An anterior approach was used in 15 subjects, and both posterior and anterior approaches were used in five subjects. RESULTS: The prefixed type plexus formation was observed in eight cases (40%). In these cases, S(1) and S(2)

roots contributed to the formation of the pudendal nerve. In the postfixed type, the S(3) root was dominant in two cases (66.7%), and less the S(4) root in one case (23.3%), albeit to a lesser degree. Most commonly, the S(2) root participated in its formation in 17 cases (85%). The inferior rectal nerve penetrating the sacrospinous ligament was seen in one case, arising from the pudendal nerve before entering the pudendal canal in four cases. The dorsal nerve of the penis arose from the S(1) root in two cases (10%). We observed it branching before entering the pudendal canal in 15 cases (75%), and it had divided in the pudendal canal in the other cases. For the posterior access, the pudendal nerve was localized 13.1 ± 0.72 cm medial to the greater trochanter, 8.1 ± 0.72 cm above the ischial tuberosity, at a depth of 6.4 ± 0.32 cm. CONCLUSIONS: This description may be useful when carrying out a pudendal nerve block and during surgical procedures carried out in this anatomical region.

Chronic Pain

Functional somatic syndromes: Sensitivities and specificities of self-reports of physician diagnosis.
Warren JW, Clauw DJ
Psychosom Med. 2012 Oct 15. [Epub ahead of print]

OBJECTIVE: Functional somatic syndromes have no laboratory or pathologic abnormalities and so are diagnosed by symptom-based case definitions. However, many studies, including recent ones, have used self-reports of physician diagnosis rather than the case definitions. Our objective was to determine the sensitivities and specificities of self-report of physician diagnosis for chronic fatigue syndrome (CFS), fibromyalgia (FM), irritable bowel syndrome (IBS), panic disorder, and migraine. METHODS: Each of 312 female patients with incident interstitial cystitis/bladder pain syndrome and matched population-based controls were queried on self-report of physician diagnosis and separately on established case definitions for each of these syndromes. RESULTS: Using the symptom-based case definitions as standards, we found that self-report of physician diagnosis did not identify 90% of the controls who had CFS, 77% who had FM, 69% who had IBS, 43% who had panic disorder, and 23% who had migraine. In addition, it missed most individuals with multiple syndromes. Findings in one cohort (controls) were confirmed in another (patients with interstitial cystitis/bladder pain syndrome). CONCLUSIONS: Self-report of physician diagnosis did not identify most of the three most venerable functional somatic syndromes, IBS, FM, and, especially, CFS; nor did it identify substantial minorities of individuals with panic disorder and migraine. Self-report of physician diagnosis was particularly poor in recognizing persons with multiple syndromes. The insensitivity of this diagnostic test has effects on not only prevalence and incidence estimates but also correlates, comorbidities, and case recruitment. To reveal individuals with these syndromes, singly or together, queries of symptoms, not diagnoses, are necessary.

Conditioned pain modulation in populations with chronic pain: A systematic review and meta-analysis.
Lewis GN, Rice DA, McNair PJ
J Pain. 2012 Sep 12. pii: S1526-5900(12)00736-5. doi: 10.1016/j.jpain.2012.07.005. [Epub ahead of print]

A systematic literature review and meta-analysis were undertaken to determine if conditioned pain modulation is dysfunctional in populations with chronic pain. Studies that used a standardized protocol to evaluate conditioned pain modulation in a chronic pain population and in a healthy control population were selected and reviewed. Thirty studies were included in the final review, encompassing data from 778 patients and 664 control participants. Across all studies there was a large effect size of .78, reflecting reduced conditioned pain modulation in the patient group. Analysis of moderator variables indicated a significant influence of participant gender and age on the effect size. Methodological moderator variables of type of outcome measure, type of test stimulus, type of conditioning stimulus, and the level of conditioning stimulus pain were not significant. A risk of bias assessment indicated that poor blinding of assessors and a lack of control of confounding variables were common. It is concluded that conditioned pain modulation is impaired in populations with chronic pain. Future studies should ensure adequate matching of participant age and gender between

patient and control groups, blinding of the assessors obtaining the outcome measures, and more rigorous control for variables known to influence the level of modulation. PERSPECTIVE: This review compared the efficacy of conditioned pain modulation between chronic pain and healthy populations. The finding of impaired modulation in the chronic pain groups highlights the dysfunction of endogenous pain modulatory mechanisms in this population.

Pain education: Getting an early start.
Hartrick CT, Rozek RJ, Conroy S, Dobritt D, Felten D
Pain Practice: 20 Jun 2012. DOI: 10.1111/j.1533-2500.2012.00581.x

In this issue of Pain Practice, Vadivelu et al. present an update on the state of pain medicine education in medical schools worldwide. In this article, the authors make a plea for pain management specialists to work with health educators to incorporate education on acute pain into medical school curricula.

Neuroimaging findings of central nervous system dysfunction in neuropathic pain.
(Article in Japanese)
Hirano S
Brain Nerve. 2012 Nov;64(11):1267-72.

The central mechanism of pain is influenced by multiple factors including the quality of stimulation, cognition, psychological status, environment, and genetics. The region of the brain modulated by painful sensation, taken together, are termed as "pain matrix," composing primary/secondary somatosensory area, thalamus, insula, prefrontal cortex, anterior cingulate cortex, basal ganglia, limbic system, brainstem, and cerebellum. The degrees of noxious stimulation and chronic spontaneous pain are associated with activity in the insula and the anterior cingulate cortex, which is involved in the emotional dimension of pain. Brain activation by allodynia is observed in the thalamus, prefrontal cortex, anterior cingulate, insula, and cerebellum and relates to attention and sensory-motor integration. Molecular neuroimaging studies indicate that the underlying pathophysiology of pain is related to the dopaminergic system, opioidergic system, and brain inflammation. Functional neuroimaging can elucidate the pathophysiology of acute and chronic pain syndromes, and thus objectively evaluate the degree of pain sensation, enabling us to plan pain control therapies for the future.

Functional limitations and physical symptoms of individuals with chronic pain.
Björnsdóttir S, Jónsson S, Valdimarsdóttir U
Scand J Rheumatol. 2012 Nov 6. [Epub ahead of print]

OBJECTIVES: Chronic pain is a debilitating condition that may cause additional symptoms affecting the sufferers' working capacity and quality of life. Studying the prevalence and consequences of chronic pain in various populations remains important for a complete picture of the global burden imposed by chronic pain conditions. METHODS: We investigated the prevalence of self-reported chronic pain conditions in Iceland in addition to symptoms and functional limitations within the group, using a population-based random sample. A questionnaire was mailed to 9807 Icelanders aged 18-79 years and, of these, 5906 participated in the study. Chronic pain was considered manifest in people reporting chronic low back pain, chronic neck symptoms, and/or fibromyalgia. Prevalence calculations were weighted with respect to gender, age, and residential area to represent the underlying population. Associations of chronic pain conditions with symptoms and functional limitations were measured with adjusted logistic regression models, contrasting symptoms in individuals reporting any of the three pain conditions with those who did not. RESULTS: The population-estimated prevalence of chronic pain condition was 19.9% with distinct gender differences (men = 15.2%, women = 24.7%). Several symptoms and functional limitations in daily life were strongly associated with chronic pain, including deficient energy and muscular discomfort, physical mobility limitations, lifting groceries, climbing stairs, and stooping. Women, but not men, with chronic pain tended to refrain from physical activity. CONCLUSIONS: Chronic pain is a prevalent condition and

those who report chronic pain generally suffer from ill health and limitations in their daily life compared to individuals not suffering from the condition.

What is spontaneous pain and who has it?
Bennett GJ
J Pain. 2012 Oct.

Spontaneous pain is often discussed in the context of both chronic inflammatory and neuropathic pain conditions, and it has been suggested that spontaneous pain, rather than stimulus-evoked pain, may be the more significant clinical problem. The following issues are discussed here. First, it is suggested that the concept of spontaneous pain makes no sense when the pain is the result of an ongoing inflammatory reaction. Evidence is reviewed that indicates that spontaneous pain is present in patients with neuropathic pain, but perhaps only in a subset of such patients. Second, it is suggested that in the presence of allodynia and hyperalgesia, stimulation from the activities of daily life occurs very many times a day and that these stimulus-evoked pains may summate to give a fluctuating level of daily pain that both patients and investigators mistake for spontaneous pain.

Elucidation of pathophysiology and treatment of neuropathic pain.
Vranken JH
Cent Nerv Syst Agents Med Chem. 2012 Oct 2. [Epub ahead of print]

Neuropathic pain, pain arising as a direct consequence of a lesion or disease affecting the somatosensory system, is relatively common, occurring in about 1% of the population. Studies in animal models describe a number of peripheral and central pathophysiological processes after nerve injury that would be the basis of underlying neuropathic pain mechanism. Additionally, neuro-imaging (positron emission tomography and functional magnetic resonance imaging) provides insights in brain mechanisms corresponding with mechanistic processes including allodynia, hyperalgesia, altered sensation, and spontaneous pain. A change in function, chemistry, and structures of neurons (neural plasticity) underlie the production of the altered sensitivity characteristics of neuropathic pain. Peripheral processes in neuropathic pain involve production of mediators (cytokines, protons, nerve growth factor), alterations in calcium channels, sodium channels, hyperpolarisation-activated nucleotide-gated ion channels, and potassium channels, phenotypic switches and sprouting of nerves endings, and involvement of the sympathetic nervous system. Stimulation of the N-Methyl-D-Aspartate receptor, activation of microglia, oligodendrocytes, and astrocytes, increased production of nerve growth factor and brain-derived neurotrophic factor together with loss of spinal inhibitory control are responsible for central neuron hyperexcitability and maintenance of neuropathic pain. Recent advances, including functional imaging techniques, in identification of peripheral and central sensitization mechanisms related to nervous system injury have increased potential for affecting pain research from both diagnostic as well as therapeutic view. Key brain regions involved in generating pharmacologically induced analgesia may be identified. Despite the progress in pain research, neuropathic pain is challenge to manage. Although numerous treatment options are available for relieving neuropathic pain, there is no consensus on the most appropriate treatment. However, recommendations can be proposed for first-line, second-line, and third-line pharmacological treatments based on the level of evidence for the different treatment strategies. Available therapies shown to be effective in managing neuropathic pain include opioids and tramadol, anticonvulsants, antidepressants, topical treatments (lidocaine patch, capsaicin), and ketamine. Tricyclic antidepressants are often the first drugs selected to alleviate neuropathic pain (first-line pharmacological treatment). Although they are very effective in reducing pain in several neuropathic pain disorders, treatment may be compromised (and outweighed) by their side effects. In patients with a history of cardiovascular disorders, glaucoma, and urine retention, pre¬gabalin and gabapentine are emerging as first-line treatment for neuropathic pain. In addition these anti-epileptic drugs have a favourable safety profile with minimal concerns regarding drug interactions and showing no interference with hepatic enzymes. Alternatively, opioids (oxycodone and methadone) and tramadol may alleviate nociceptive and neuropathic pain. Despite the numerous treatment options available for relieving neuropathic pain, no more than half of patients experience clinically meaningful pain relief, which is almost always partial but not complete relief. In addition, patients

frequently experience burdensome adverse effects and as a consequence are often unable to tolerate the treatment. In the remaining patients, combination therapies using two or more analgesics with different mechanisms of action may also offer adequate pain relief. Although combination treatment is clinical practice and may result in greater pain relief, trials regarding different combinations of analgesics are lacking (which combination to use, occurrence of additive or supra-additive effects, sequential or concurrent treat¬ment, adverse-event profiles of these analgesics, alone and in combination) are scarce. If medical treatments have failed, invasive therapies such as intrathecal drug administration and neurosurgical stimulation techniques (spinal cord stimulation, deep brain stimulation, and motor cortex stimulation) may be considered.

Capsaicin for neuropathic pain: Linking traditional medicine and molecular biology.
Haanpää M, Treede RD
Eur Neurol. 2012 Sep 28;68(5):264-275. [Epub ahead of print]

Capsaicin has long been used as a traditional medicine to treat pain and, recently, its mechanism of analgesic action has been discovered. This review article documents the clinical development of capsaicin to demonstrate that pharmacognosy still has a profound influence on modern-day drug development programs. Capsaicin is a highly selective agonist for the transient receptor potential channel vanilloid-receptor type 1 (TRPV1), which is expressed on central and peripheral terminals of nociceptive primary sensory neurons. Knockout studies have revealed the importance of TRPV1 as a molecular pain integrator and target for novel analgesic agents. Topical application of capsaicin at the peripheral terminal of TRPV1-expressing neurons superficially denervates the epidermis in humans in a highly selective manner and results in hypoalgesia. In three recent randomized controlled trials, a patch containing high-concentration capsaicin demonstrated meaningful efficacy and tolerability relative to a low-concentration capsaicin control patch in patients with peripheral neuropathic pain. Data from clinical practice will determine if the high-concentration capsaicin patch is effective in real-world settings.

Pain is associated with short leukocyte telomere length in women with fibromyalgia.
Hassett AL, Epel E, Clauw DJ, Harris RE, Harte SE, Kairys A, Buyske S, Williams DA
J Pain. 2012 Oct.

Telomere length, considered a measure of biological aging, is linked to morbidity and mortality. Psychosocial factors associated with shortened telomeres are also common in chronic pain; yet, little is known about telomere length in pain populations. Leukocyte telomere length was evaluated in 66 women with fibromyalgia and 22 healthy female controls. Participants completed questionnaires and a subgroup of fibromyalgia patients underwent quantitative sensory testing (QST; n = 12) and neuroimaging (n = 12). Telomere length was measured using the quantitative polymerase chain reaction method. Although patients had shorter telomere length than controls, the difference was not statistically significant. However, higher levels of pain within fibromyalgia were associated with shorter telomere length (P = .039). When pain and depression were combined, patients categorized as high-pain/high-depression had an age-adjusted telomere length 265 base pairs shorter than those with low-pain/low-depression (P = .043), a difference consistent with approximately 6 years of chronological aging. In the subset tested, telomere length was also related to pain threshold and pain sensitivity, as well as gray matter volume, such that patients with shorter telomeres were more sensitive to evoked pain and had less gray matter in brain regions associated with pain processing (eg, primary somatosensory cortex). These preliminary data support a relationship between pain and telomere length.

The glutamatergic system as a target for neuropathic pain relief.
Osikowicz M, Mika J, Przewlocka B
Exp Physiol. 2012 Sep 21. [Epub ahead of print]

Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system. The understanding of glutamatergic transmission in the nervous system has been greatly expanded with the discovery and investigation of the family of ionotropic and metabotropic glutamate receptors (GluRs). Metabotropic glutamate receptors are localised at nerve terminals, postsynaptic sites and glial cells and thus, they can influence and modulate the action of glutamate at different levels in the synapse. Moreover, there is substantial evidence of glial participation in glutamate nociceptive processes and neuropathic pain. Metabotropic glutamate receptors have been shown to play a role in neuropathic pain, which is one of the most troublesome illnesses because the therapy is still not satisfactory. Recently, the development of selective mGluR ligands has provided important tools for further investigation of the role of mGluRs in the modulation of chronic pain processing. This paper presents a review of the literature of glutamate receptors in neuropathic pain and the role of glia in these effects. Specifically, pharmacological interventions aimed at inhibiting group I mGlu, and/or potentiating group II and III mGluR-mediated signalling is discussed. Moreover we introduce the data about the role of glutamate transporters. They are responsible for the level of glutamate in the synaptic cleft and thus regulate the effects of all three groups of mGlu receptors and in consequence the activity of this system in nociceptive transmission. Additionally, the question of how the modulation of the glutamatergic system influences the effectiveness of analgesic drugs used in neuropathic pain therapy will be addressed.

Motor cortex stimulation inhibits thalamic sensory neurons and enhances activity of PAG neurons: Possible pathways for antinociception.
Pagano RL, Fonoff ET, Dale CS, Ballester G, Teixeira MJ, Britto LR
Pain. 2012 Sep 24. pii: S0304-3959(12)00473-3. doi: 10.1016/j.pain.2012.08.002. [Epub ahead of print]

Motor cortex stimulation is generally suggested as a therapy for patients with chronic and refractory neuropathic pain. However, the mechanisms underlying its analgesic effects are still unknown. In a previous study, we demonstrated that cortical stimulation increases the nociceptive threshold of naive conscious rats with opioid participation. In the present study, we investigated the neurocircuitry involved during the antinociception induced by transdural stimulation of motor cortex in naive rats considering that little is known about the relation between motor cortex and analgesia. The neuronal activation patterns were evaluated in the thalamic nuclei and midbrain periaqueductal gray. Neuronal inactivation in response to motor cortex stimulation was detected in thalamic sites both in terms of immunolabeling (Zif268/Fos) and in the neuronal firing rates in ventral posterolateral nuclei and centromedian-parafascicular thalamic complex. This effect was particularly visible for neurons responsive to nociceptive peripheral stimulation. Furthermore, motor cortex stimulation enhanced neuronal firing rate and Fos immunoreactivity in the ipsilateral periaqueductal gray. We have also observed a decreased Zif268, δ-aminobutyric acid (GABA), and glutamic acid decarboxylase expression within the same region, suggesting an inhibition of GABAergic interneurons of the midbrain periaqueductal gray, consequently activating neurons responsible for the descending pain inhibitory control system. Taken together, the present findings suggest that inhibition of thalamic sensory neurons and disinhibition of the neurons in periaqueductal gray are at least in part responsible for the motor cortex stimulation-induced antinociception.

The posterior insular-opercular region and the search of a primary cortex for pain.
Garcia-Larrea L
Neurophysiol Clin. 2012 Oct;42(5):299-313. doi: 10.1016/j.neucli.2012.06.001.

To be considered specific for nociception, a cortical region should: (a) have plausible connections with ascending nociceptive pathways; (b) be activated by noxious stimuli; (c) trigger nociceptive sensations if directly stimulated; and (d) tone down nociception when injured. In addition, lesions in this area should have a potential to develop neuropathic pain, as is the case of all lesions in nociceptive pathways. The single cortical region approaching these requirements in

humans encompasses the suprasylvian posterior insula and its adjoining medial operculum (referred to as "PIMO" in this review). This region does not contain, however, solely nociceptive networks, but represents in primates the main sensory receiving area of the spinothalamic system, and as such contributes to the processing of thermo-sensory, nociceptive, C-fibre tactile, and visceral input. Nociception (and, a fortiori, pain) should therefore not be considered as a separate sensory modality, like vision or audition, but rather as one component of a global system subtending the most primitive forms of somatosensation. Although a clear functional segregation of PIMO sub-areas has not yet been achieved, some preferential distribution has been described in humans: pain-related networks appear preferentially distributed within the posterior insula, and non-noxious thermal processing in the adjacent medial operculum. Thus, spinothalamic sub-modalities may be partially segregated in the PIMO, in analogy with the separate representation of dorsal column input from joint, muscle spindle and tactile afferents in S1. Specificity, however, may not wholly depend on ascending 'labelled lines' but also on cortical network properties driven by intrinsic and extrinsic circuitry. Given its particular anatomo-functional properties, thalamic connections, and tight relations with limbic and multisensory cortices, the PIMO region deserves to be considered as a third somatosensory region (S3) devoted to the processing of spinothalamic inputs.

Sex and gender aspects in anesthetics and pain medication.
Campesi I, Fois M, Franconi F
Handb Exp Pharmacol. 2012;(214):265-78. doi: 10.1007/978-3-642-30726-3_13.

The influence of sex and gender on anesthesia and analgesic therapy remains poorly understood, nevertheless the numerous physiological and pharmacological differences present between men and women. Although in anesthesiology sex-gender aspects have attracted little attention, it has been reported that women have a greater sensitivity to the non-depolarizing neuroblocking agents, whereas males are more sensitive than females to propofol. It has been suggested that men wake slower than women after general anesthesia and have less postoperative nausea and vomiting. Sexual hormones seem to be of importance in the onset of differences. Nevertheless, in the last years, sex-gender influences on pain and analgesia have become a hot topic and data regarding sex-gender differences in response to pharmacologic and non-pharmacologic pain treatments are still scanty, inconsistent, and non-univocal. In particular, females seem to be more sensitive than males to opioid receptor agonists. Women may experience respiratory depression and other adverse effects more easily if they are given the same doses as males. Evidently, there is an obvious need for more research, which should include psychological and social factors in experimental preclinical and clinical paradigms in view of their importance on pain mechanism, in order to individualize analgesia to optimize pain relief.

Cognitive function in patients with chronic pain treated with opioids: characteristics and associated factors.
Kurita GP, DE Mattos Pimenta CA, Braga PE, Frich L, Jørgensen MM, Nielsen PR, Højsted J, Sjøgren P
Acta Anaesthesiol Scand. 2012 Sep 4. doi: 10.1111/j.1399-6576.2012.02760.x. [Epub ahead of print]

BACKGROUND: The paucity of studies regarding cognitive function in patients with chronic pain, and growing evidence regarding the cognitive effects of pain and opioids on cognitive function prompted us to assess cognition via neuropsychological measurement in patients with chronic non-cancer pain treated with opioids. METHODS: In this cross-sectional study, 49 patients were assessed by Continuous Reaction Time, Finger Tapping, Digit Span, Trail Making Test-B and Mini-mental State Examination tests. Linear regressions were applied. RESULTS: Patients scored poorly in the Trail Making Test-B (mean = 107.6 s, SD = 61.0, cut-off = 91 s); and adequately on all other tests. Several associations among independent variables and cognitive tests were observed. In the multiple regression analyses, the variables associated with statistically significant poor cognitive performance were female sex, higher age, lower annual income, lower schooling, anxiety, depression, tiredness, lower opioid dose, and more than 5 h of sleep the night before assessment ($P < 0.05$). CONCLUSIONS: Patients with chronic pain may have cognitive dysfunction related to some reversible factors, which can be optimized by therapeutic interventions.

Prospective study of 3-year follow-up of low-dose intrathecal opioids in the management of chronic nonmalignant pain.

Hamza M, Doleys D, Wells M, Weisbein J, Hoff J, Martin M, Soteropoulos C, Barreto J, Deschner S, Ketchum J
Pain Med. 2012 Oct;13(10):1304-13. doi: 10.1111/j.1526-4637.2012.01451.x.

OBJECTIVE: Long-term follow-up with the use of low-dose opioids in intrathecal (IT) drug delivery system (DDS) for the treatment of intractable, severe chronic nonmalignant pain. DESIGN: This is a prospective, cohort long-term outcome study. INTERVENTION: The intervention was the implantation of DDS. METHODS AND PATIENTS: A total of 61 consecutive patients (60% females, 40% males) with a mean age of 59.2 years and a mean duration of symptoms prior to implant of 6.2 years were referred for implant of DDS for severe intractable noncancer pain. After adequate patient evaluation, each underwent a trial with IT opioids. Three patients failed the trial and 58 patients were implanted. Follow-up was 36 months, with intervals at 6, 12, 18, 24, and 36 months. The Brief Pain Inventory was used for follow-up assessment criteria at baseline prior to implant as well as throughout the duration of the study. OUTCOME MEASURES: Outcome measures included self-reported pain scores (worst and average), functional improvement, and IT dose, and oral opioid consumption. RESULTS: We observed a statistically significant reduction in both worst and average pain from baseline (8.91 and 7.47 at baseline) throughout the duration of the study (4.02 and 3.41, respectively, at 36 months) ($P = 0.012$ and $P < 0.001$, respectively). We also documented a statistically significant improvement in physical and behavioral function. All subjects showed a significant reduction in the oral opioid consumption. The dose of IT opioids remained low and virtually unchanged for 36 months of follow-up: 1.4 morphine equivalent/day at 6 months and 1.48 at 36 months. Oral opioid averaged 128.9 mg of morphine equivalent/patient/day at baseline to 3.8 at 3 month and remained at the same level throughout the study. CONCLUSION: Low-dose IT opioid can provide sustained significant improvement in pain and function for long-term follow-up in chronic noncancer pain.

Clinical outcomes of multidisciplinary pain rehabilitation among African American compared with Caucasian patients with chronic pain.

Hooten WM, Knight-Brown M, Townsend CO, Laures HJ
Pain Med. 2012 Sep 19. doi: 10.1111/j.1526-4637.2012.01489.x. [Epub ahead of print]

OBJECTIVES: The primary aim of this study was to determine if the immediate outcomes of multidisciplinary pain rehabilitation were different for African Americans compared with Caucasians. DESIGN: A retrospective repeated measures design was used, and all analyses were adjusted for marital and employment status, years of education, and pain duration. SETTING: Multidisciplinary pain rehabilitation center. SUBJECTS: Each African American (N = 40) consecutively admitted to a multidisciplinary pain rehabilitation program was matched with three Caucasians (N = 120) on age, sex, and treatment dates. INTERVENTION: A 3-week outpatient multidisciplinary pain rehabilitation program. OUTCOME MEASURES: The Multidimensional Pain Inventory, Short Form-36 Health Status Questionnaire, Center for Epidemiologic Studies-Depression scale, and Pain Catastrophizing Scale were administered at admission and dismissal. RESULTS: At baseline, African Americans had greater pain severity ($P < 0.001$) and poorer physical function compared with Caucasians ($P < 0.001$). At program completion, African Americans had greater pain severity ($P < 0.001$) and poorer measures of life interference ($P = 0.004$), perceived control ($P = 0.013$), affective distress ($P < 0.001$), role physical ($P = 0.001$) and role emotional function ($P = 0.001$), physical ($P < 0.001$) and social function ($P = 0.002$), general health ($P = 0.005$), depression ($P < 0.001$), and pain catastrophizing ($P < 0.001$). A repeated measures analysis demonstrated a time by race interaction effect for pain interference ($P = 0.038$), affective distress ($P = 0.019$), role physical function ($P = 0.007$), social function ($P = 0.029$), and depression ($P = 0.004$), indicating African Americans experienced less improvement compared with Caucasians. CONCLUSIONS: The results of this study highlight an under-recognized health disparity which provides the basis for developing targeted interventions aimed at improving the clinical outcomes of African Americans with chronic pain.

Chronic pain is more than a peripheral event.
Loeser JD
J Pain. 2012 Oct.

No Abstract Available.

Vulvovaginal Disorders

Effect of lubricating gel on patient comfort during vaginal speculum examination: a randomized controlled trial.
Hill DA, Lamvu G
Obstet Gynecol. 2012 Feb;119(2 Pt 1):227-31.

OBJECTIVE: To estimate the efficacy of lubricating gel compared with using water for pain during vaginal speculum insertion. METHODS: This study was a randomized trial of nonpregnant women aged 18-50 years who required a vaginal speculum examination between February and July 2011. Patients blinded to study assignment underwent vaginal speculum examination using a standardized technique with a medium-sized plastic speculum prepared with either 0.3 mL lubricating gel or 3 mL of water used to cover both speculum blades. Patients recorded pain using a 10-cm visual analog scale immediately after speculum insertion. A pre hoc power analysis determined that 55 patients in each arm would be required to detect a difference of 0.9 cm on a 10-cm visual analog scale. RESULTS: A total of 299 consecutive women requiring vaginal speculum examination were screened for enrollment and 120 women were randomized with 60 per group. There were no marked differences in the demographic characteristics of the gel (n=59) and water (n=60) participants available for final analysis. The gel group showed significantly lower pain scores for speculum insertion (mean ± standard deviation: 1.41±1.55 compared with water 2.15±1.93, P<.01). Of patients undergoing examination with gel, 20 of 59 (33.9%) marked zero on the pain scale compared with six of 60 (10%) patients receiving water (P=.002). All 73 patients who underwent Pap screening had adequate cytology. CONCLUSION: Applying a small amount of lubricating gel significantly decreases patient pain during vaginal speculum insertion.

Quantification of normal vaginal constituents using a new wet preparation technique.
Fowler RS
J Low Genit Tract Dis. 2012 Oct;16(4):437-41. doi: 10.1097/LGT.0b013e31825a8b08.

OBJECTIVE: This study aimed to evaluate a new method for preparing vaginal wet preparations to enable quantification of cells and lactobacilli. The current nonstandardized technique allows for a variable amount of vaginal fluid collected, diluted by a variable amount of saline/KOH, and no quantification of constituents. MATERIALS: The vaginal fluids from 100 randomly selected women without vulvovaginitis symptoms presenting to the author's practice at Mayo Clinic underwent analysis by the quantification technique. Women were excluded if they were younger than 18 years, had antibiotics within the past 2 months, currently on their period, had placed anything in the vagina for the past 24 hours, used Depo-Provera, or were lactating. METHODS: All the wet preparations were made by mixing the natural vaginal fluids with 3 mL of sterile normal saline. Spinal diluting fluid was added to the saline preparation. The saline and KOH mixtures were injected into separate wells of KOVA Glasstic Grid Slide and analyzed with a phase-contrast microscope at 40× and 60×. The concentration of leukocytes, lactobacilli, and squamous cells and the degree of maturation of the majority (>50%) of squamous cells were assessed, and it was determined whether there was excessive non-lactobacilli bacteria (EB) as evident by clumps of bacteria in the background fluid and speckling on the squamous cells. RESULTS: The 3 most common patterns to occur were as follows: First, 51% (95% confidence interval [CI] = 41%-60%) of the total specimens had abundant lactobacilli, no leukocytes, more than 50% fully maturated squamous cells, and no EB. Second, 22% (95% CI = 14%-32%) of the total specimens had low lactobacilli counts, no leukocytes, more than 50% undermaturated squamous cells, and no EB. Third, 12% (95% CI = 6%-20%) of the total specimens had abundant

lactobacilli, leukocytes, more than 50% fully maturated squamous cells, and no EB. CONCLUSIONS: It is imperative to be able to objectively quantify normal vaginal secretion constituents so that (1) the abnormal patterns can be demarcated and (2) treatment targets of what constitutes healthy vaginal conditions can be provided.

The role of physical examination in diagnosing common causes of vaginitis: a prospective study.
Singh RH, Zenilman JM, Brown KM, Madden T, Gaydos C, Ghanem KG
Sex Transm Infect. 2012 Sep 27. [Epub ahead of print]

OBJECTIVE: We evaluated agreement in diagnoses for bacterial vaginosis (BV), Trichomonas vaginalis (TV) and vulvovaginal candidiasis (VVC) between clinicians examining the patient and performing diagnostic tests versus a clinician with access only to the patient's history and diagnostic findings from self-obtained vaginal swabs (SOVS). DESIGN: Women presenting with vaginal discharge to a sexually transmitted infections clinic provided SOVS for evaluation and completed the study and qualitative questionnaires. A clinician then obtained a history and performed speculum and bimanual examinations. Participants' history and diagnostic test results from SOVS were provided to a masked non-examining clinician who rendered independent diagnoses. Overall agreement in diagnoses and κ statistics was calculated. RESULTS: The prevalence of infections among the 197 participants was 63.4% (BV), 19% (TV) and 14% (VVC). The percent agreement between the examining and non-examining clinician for the diagnoses of BV was 68.5%, 90.9% for TV and 91.9% for VVC. Of the 105 women diagnosed with BV by the examining clinician, 34 (32%) were missed by the non-examining clinician. The non-examining clinician missed 13 (48%) of 27 women and 12 (34%) of 35 women treated for VVC and TV, respectively. Four women who all presented with abdominal pain were diagnosed with pelvic inflammatory disease. CONCLUSIONS: Tests from SOVS and history alone cannot be used to adequately diagnose BV, TV and VVC in women presenting with symptomatic vaginal discharge. Cost benefits from eliminating the speculum examination and using only tests from SOVS may be negated by long-term costs of mistreatment.

Aerobic vaginitis and mixed infections: comparison of clinical and laboratory findings.
Fan A, Yue Y, Geng N, Zhang H, Wang Y, Xue F
Arch Gynecol Obstet. 2012 Sep 27. [Epub ahead of print]

PURPOSE: To investigate the clinical features of aerobic vaginitis (AV) and mixed infections with AV to achieve efficient diagnosis. METHODS: From April 2008 to August 2009, 657 consecutive outpatients with vaginal symptoms in gynecology clinic in the General Hospital of Tianjin Medical University were investigated. Samples were taken for examination of vaginal discharge and fresh wet mount microscopy. AV, bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomonal vaginitis (TV) were diagnosed according to standardized definitions. Sixty patients with single AV were randomly selected over the same period. Each patient accepted moxifloxacin therapy. Two kinds of treatment course (400 mg qd, 6 days or 400 mg qd, 12 days) were given. Clinical features and laboratory test results in the first visit and follow-ups were recorded and statistically analyzed. RESULT: Among the 657 cases, AV was found in 23.74 % of the cases (156/657). AV mixed infections were diagnosed in 53.85 % (84/156): the mixed infections included VVC (32/84, 38.10 %), BV (31/84, 36.90 %), and TV (21/84, 25.00 %). Common symptoms of AV were a change in the characteristics of the discharge (44/72, 61.11 %) and increased discharge (30/72, 41.67 %). Vaginal pH was usually higher than 4.5 (63/72, 87.50 %). Enterococcus faecalis, Streptococcus viridans, Escherichia coli, and Staphylococcus epidermidis were frequently isolated. There is no statistically significant difference between two moxifloxacin treatment groups ($p > 0.05$). Cure rate was 89.7 % in 6-day group, and 71.4 % in 12-day group. CONCLUSIONS: AV is a common vaginal infection, and it is often mixed with other infections, especially VVC, BV and TV. The symptoms and signs of AV mixed infections are atypical. If a patient has vaginal complaints, it is necessary to determine whether AV or mixed infections are present. Oral moxifloxacin is effective in treating AV, and an appropriate course should be selected taking the severity of AV into consideration.

Comparison between Fluconazole with oral protexin combination and Fluconazole in the treatment of vulvovaginal Candidiasis.

Nouraei S, Amir Ali Akbari S, Jorjani M, Alavi Majd H, Afrakhteh M, Ghafoorian A, Tafazzoli Harandi H

ISRN Obstet Gynecol. 2012;2012:375806. doi: 10.5402/2012/375806.

BACKGROUND: According to the limited studies reporting new treatments for vulvovaginal candidiasis, this study was designed to compare the combination of fluconazole and oral protexin with fluconazole in the treatment of vulvovaginal candidiasis. METHODS: A double-blind clinical trial was conducted, involving 90 women who were referred to the gynecology clinic. Vulvovaginal candidiasis was diagnosed with itching, cheesy vaginal discharge, and any one of the following: dysuria, pH < 4.5, dyspareunia, vulvar erythema, or vulvar edema and if branched hyphae and Candida buds were visible after addition of KOH 10% in the culture and the result of cultivation in Sabouraud's dextrose agar medium was positive. Patients were randomly classified into two groups Absence of discharge, itching, and negative culture results 5-7 days after completion of treatment indicated treatment success. Data in this study were analyzed using the SPSS version 17.0 software. RESULTS: The combinations, fluconazole-oral protexin and fluconazole-placebo, were equally effective in reduction of complaints and symptoms, but fluconazole-oral protexin combination elicited a better therapeutic response ($\chi(2) = 0.01$, $P = 6.7$). In addition, fluconazole-oral protexin combination treatment demonstrated better recovery time ($t = -2.04$, $P = 0.04$). CONCLUSIONS: This study demonstrated that complementary treatment with probiotic Lactobacillus increased the efficacy of fluconazole in treatment of vulvovaginal candidiasis. Further research is recommended.

Vaginal infections update.

Mashburn J

J Midwifery Womens Health. 2012 Oct 24. doi: 10.1111/j.1542-2011.2012.00246.x. [Epub ahead of print]

Vaginal symptoms are one of the leading reasons that women visit their health care providers. Women often self-diagnose and may treat themselves inappropriately. This article describes the etiology, risk factors, symptoms, diagnosis, and treatment of the 3 most common vaginal infections: bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis.

Common vulvar dermatologic conditions.

(Article in Finnish)

Hiltunen-Back E, Jeskanen L

Duodecim. 2012;128(17):1763-9.

A wide range of cutaneous diseases can affect genital area. Some of these dermatoses are predominantly present in vulvar area while others primarily occur in extra-genital skin areas. Genital area is susceptible to maceration and the combination of moisture and warmth together with the increased penetration of topical agents make the region vulnerable for mechanical and chemical irritation. Lichen simplex chronicus (LSC) is a secondary condition precipitated by chronic itching and scratching. Scratching may be caused by some dermatoses or candida infection. Chronic systemic dermatoses most commonly affecting vulval area are various eczemas, psoriasis, lichen sclerosus and lichen planus.

Psoriasis and concomitant fibrosing disorders: Lichen sclerosus, morphea, and systemic sclerosis.

Walls AC, Qureshi AA

J Am Acad Dermatol. 2012 Nov;67(5):1079-83. doi: 10.1016/j.jaad.2012.04.031.

No Abstract Available.

Expression of human telomerase reverse transcriptase in vulvar intraepithelial neoplasia and squamous cell carcinoma: An immunohistochemical study with survivin and p53.

Wellenhofer A, Brustmann H

Arch Pathol Lab Med. 2012 Nov;136(11):1359-65. doi: 10.5858/arpa.2011-0440-OA.

CONTEXT: Human telomerase reverse transcriptase (hTERT), an enzyme that enables cells to overcome replicative senescence and to divide indefinitely, is overexpressed in many cancers and their precursor lesions. OBJECTIVE: To test whether hTERT expression is related to neoplastic progression and resistance to apoptosis in vulvar epithelia. DESIGN: Immunoexpression of hTERT was evaluated in 101 formalin-fixed, paraffin-embedded archival vulvar epithelia consisting of normal squamous vulvar epithelia (n = 25), lichen sclerosus (n = 10), high-grade classic vulvar intraepithelial neoplasia (n = 16), differentiated vulvar intraepithelial neoplasia (n = 18), and vulvar invasive keratinizing squamous cell carcinoma (n = 32) and related to survivin and p53 expression. Immunostaining for all factors was scored for moderate and strong intensities with regard to quantity to determine upregulation and overexpression (score 0, 0% immunoreactive cells; score 1+, <5% immunoreactive cells; score 2+, 5% to 50% immunoreactive cells; score 3+, >50% immunoreactive cells). Score 3+ was considered as overexpression. RESULTS: Nuclear hTERT immunoexpression was closely related to survivin reactivity, increased from normal vulvar squamous epithelia to lichen sclerosus and to high-grade classic vulvar intraepithelial neoplasia, differentiated vulvar intraepithelial neoplasia, and invasive keratinizing squamous cell carcinoma ($P < .001$), and followed the morphologic distribution of atypical squamous epithelial cells. Overexpression of hTERT was comparable to that seen for p53 in invasive keratinizing squamous cell carcinoma ($P = .62$); significant differences were calculated for differentiated vulvar intraepithelial neoplasia ($P = .003$) and high-grade classic vulvar intraepithelial neoplasia ($P = .001$). CONCLUSION: Human telomerase reverse transcriptase is upregulated in vulvar intraepithelial neoplasia and invasive keratinizing squamous cell carcinoma compared with nonneoplastic squamous epithelia of the vulva as an apparently early and preinvasive event in the neoplastic transformation, with development of cellular longevity and resistance to apoptosis by survivin activation as associated features, independent of the etiology of vulvar intraepithelial neoplasia.

Safety and efficacy of topical Cidofovir to treat high-grade perianal and vulvar intraepithelial neoplasia in HIV-positive men and women.

Stier EA, Goldstone SE, Einstein MH, Jay N, Berry JM, Wilkin T, Lee JY, Darragh TM, Costa MD, Panther L, Aboulafia D, Palefsky JM

AIDS. 2012 Oct 1. [Epub ahead of print]

OBJECTIVE: To evaluate the safety and efficacy of topical cidofovir for treatment of high-grade squamous perianal and vulvar intraepithelial neoplasia (PAIN and VIN) lesions in HIV-positive individuals. DESIGN: Phase IIa prospective multicenter trial conducted at eight clinical sites through the AIDS Malignancy Consortium (AMC) METHODS: HIV-positive patients with biopsy-proven high-grade PAIN that was ≥ 3 cm were enrolled. PAIN biopsy specimens were assessed for HPV using PCR and type-specific HPV probing. Subjects applied 1% topical cidofovir to PAIN and VIN (if present) for 6 two-week cycles. Results were designated as complete response (CR), partial response (PR) (> 50% reduction in size), stable disease (SD), or progressive disease (PD). RESULTS: Twenty-four men and 9 women (8 with high-grade VIN as well) were enrolled. Mean age was 44 years, mean CD4+ count was 412 cells/μl. HPV DNA (most commonly HPV16) was detected in all pre-treatment study specimens. Twenty six (79%) subjects completed treatment per protocol-CR: 5 (15%); PR: 12 (36%), SD: 7 (21%); PD: 2 (6%) (1 with a superficially invasive cancer and 1 with new area of high-grade PAIN). Treatment was well tolerated with most common adverse events being mild to moderate affecting lesional skin: pain/burning/irritation (25 subjects) and ulceration (13 subjects). CONCLUSIONS: Topical cidofovir had 51% efficacy in the short-term treatment of high-grade PAIN and VIN with acceptable toxicity in HIV-positive individuals. Randomized control studies with more prolonged treatment courses and longer follow-up to assess the durability of the response are needed.

Cancer of the vulva.
Hacker NF, Eifel PJ, van der Velden J
Int J Gynaecol Obstet. 2012 Oct;119 Suppl 2:S90-6. doi: 10.1016/S0020-7292(12)60021-6.

No Abstract Available.

Metastatic bone involvement in vulvar cancer: report of a rare case and review of the literature.
Tolia M, Tsoukalas N, Platoni K, Dilvoi M, Pantelakos P, Kelekis N, Kouloulias V
Eur J Gynaecol Oncol. 2012;33(4):411-3.

PURPOSE: Bone metastasis secondary to vulvar carcinoma is an infrequent clinical entity. Only ten cases have been published in the literature. We describe a case of squamous vulvar carcinoma, that presented with cervical vertebral involvement, as a part of distant spread. CASE: A 69-year-old woman presented with radicular pain and a painful cervical mass. MRI of the cervical spine was performed, showing an osteolytic lesion with spinal cord compression. CONCLUSION: This case was unique in presenting vertebral metastasis eight months after chemotherapy and radiotherapy.

Cancer of the vagina.
Hacker NF, Eifel PJ, van der Velden J
Int J Gynaecol Obstet. 2012 Oct;119 Suppl 2:S97-9. doi: 10.1016/S0020-7292(12)60022-8.

No Abstract Available.

Pathology of cancers of the female genital tract.
Prat J
Int J Gynaecol Obstet. 2012 Oct;119 Suppl 2:S137-50. doi: 10.1016/S0020-7292(12)60027-7.

No Abstract Available.