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Feature Article

A subpopulation of nociceptors specifically linked to itch.

Han L, Ma C, Liu Q, Weng HJ, Cui Y, Tang Z, Kim Y, Nie H, Qu L, Patel KN, Li Z, McNeil B, He S, Guan Y, Xiao B, Lamotte RH, Dong X

Nat Neurosci. 2012 Dec 23. doi: 10.1038/nn.3289. [Epub ahead of print]

Itch-specific neurons have been sought for decades. The existence of such neurons has been doubted recently as a result of the observation that itch-mediating neurons also respond to painful stimuli. We genetically labeled and manipulated MrgprA3(+) neurons in the dorsal root ganglion (DRG) and found that they exclusively innervated the epidermis of the skin and responded to multiple pruritogens. Ablation of MrgprA3(+) neurons led to substantial reductions in scratching evoked by multiple pruritogens and occurring spontaneously under chronic itch conditions, whereas pain sensitivity remained intact. Notably, mice in which TRPV1 was exclusively expressed in MrgprA3(+) neurons exhibited itch, but not pain, behavior in response to capsaicin. Although MrgprA3(+) neurons were sensitive to noxious heat, activation of TRPV1 in these neurons by noxious heat did not alter pain behavior. These data suggest that MrgprA3 defines a specific subpopulation of DRG neurons mediating itch. Our study opens new avenues for studying itch and developing anti-pruritic therapies.

Vulvodynia /Vulvovaginal Pain

Evidence for overlap between urological and nonurological unexplained clinical conditions.

Rodríguez MÁ, Afari N, Buchwald DS

J Urol. 2013 Jan;189(1 Suppl):S66-74. doi: 10.1016/j.juro.2012.11.019.

PURPOSE: Unexplained clinical conditions share common features such as pain, fatigue, disability out of proportion to physical examination findings, inconsistent laboratory abnormalities, and an association with stress and psychosocial factors. We examined the extent of the overlap among urological and nonurological unexplained clinical conditions characterized by pain. We describe the limitations of previous research and suggest several possible explanatory models. MATERIALS AND METHODS: Using hallmark symptoms and syndromes as search terms a search of 12 databases identified a total of 1,037 full-length published articles in 8 languages from 1966 to April 2008. The search focused on the overlap of chronic pelvic pain, interstitial cystitis, painful bladder syndrome, chronic prostatitis/chronic pelvic pain syndrome or vulvodynia with fibromyalgia, chronic fatigue syndrome, temporomandibular joint and muscle disorders or irritable bowel syndrome. We abstracted information on authorship, type of case and control groups, eligibility criteria,

case definitions, study methods and major findings. RESULTS: The literature suggests considerable comorbidity between urological and nonurological unexplained clinical conditions. The most robust evidence for overlap was for irritable bowel syndrome and urological unexplained syndromes with some estimates of up to 79% comorbidity between chronic pelvic pain and symptoms of irritable bowel syndrome. However, most studies were limited by methodological problems, such as varying case definitions and selection of controls. CONCLUSIONS: The overlap between urological and selected nonurological unexplained clinical conditions is substantial. Future research should focus on using standardized definitions, and rigorously designed, well controlled studies to further assess comorbidity, clarify the magnitude of the association and examine common pathophysiological mechanisms.

Vulvodynia: a case series of a poorly recognized entity.
Patsatsi A, Vavilis D, Theodoridis TD, Kellartzis D, Sotiriadis D, Tarlatzis BC
Clin Exp Obstet Gynecol. 2012;39(3):330-2.

Vulvodynia remains a poorly recognized entity with unclear pathogenesis. In a case series of six patients with vulvodynia over a five-year period in a tertiary university hospital, we describe the clinical features, the diagnostic procedures, the impact on each patient's emotional status and discuss the necessity and efficacy of the chosen treatment options in accordance with the current therapeutic guidelines.

Vestibulodynia (vulvar vestibulitis, provoked localized vulvodynia).
Trifiro M, Wallach S
J Sex Med. 2012 Dec;9(12):3285-6. doi: 10.1111/jsm.12020.

No Abstract Available.

Bone morphogenetic protein 4 mediates estrogen-regulated sensory axon plasticity in the adult female reproductive tract.
Bhattacherjee A, Rumi MA, Staecker H, Smith PG
J Neurosci. 2013 Jan 16;33(3):1050-61. doi: 10.1523/JNEUROSCI.1704-12.2013.

Peripheral axons are structurally plastic even in the adult, and altered axon density is implicated in many disorders and pain syndromes. However, mechanisms responsible for peripheral axon remodeling are poorly understood. Physiological plasticity is characteristic of the female reproductive tract: vaginal sensory innervation density is low under high estrogen conditions, such as term pregnancy, whereas density is high in low-estrogen conditions, such as menopause. We exploited this system in rats to identify factors responsible for adult peripheral neuroplasticity. Calcitonin gene-related peptide-immunoreactive sensory innervation is distributed primarily within the vaginal submucosa. Submucosal smooth muscle cells express bone morphogenetic protein 4 (BMP4). With low estrogen, BMP4 expression was elevated, indicating negative regulation by this hormone. Vaginal smooth muscle cells induced robust neurite outgrowth by cocultured dorsal root ganglion neurons, which was prevented by neutralizing BMP4 with noggin or anti-BMP4. Estrogen also prevented axon outgrowth, and this was reversed by exogenous BMP4. Nuclear accumulation of phosphorylated Smad1, a primary transcription factor for BMP4 signaling, was high in vagina-projecting sensory neurons after ovariectomy and reduced by estrogen. BMP4 regulation of innervation was confirmed in vivo using lentiviral transduction to overexpress BMP4 in an estrogen-independent manner. Submucosal regions with high virally induced BMP4 expression had high innervation density despite elevated estrogen. These findings show that BMP4, an important factor in early nervous system development and regeneration after injury, is a critical mediator of adult physiological plasticity as well. Altered BMP4 expression may therefore contribute to sensory hyperinnervation, a hallmark of several pain disorders, including vulvodynia.

Current situation: lower genital tract pathology and colposcopy training in Spanish gynecology and obstetrics residents.

Rodríguez-Mias NL, Cortés J, Xercavins J, Lailla JM

J Low Genit Tract Dis. 2013 Jan;17(1):12-6. doi: 10.1097/LGT.0b013e318259a426.

OBJECTIVE: This study aimed to evaluate the impact of an educational intervention in lower genital tract pathology (LGTP) on the knowledge and skills acquired by the Spanish specialist residents. This didactic change was carried out under the auspices of the Asociación Española de Patología Cervical y Colposcopia and the Sociedad Española Ginecología y Obstetricia and its Resident Section. STUDY DESIGN: This is an observational, descriptive, and cross-sectional study. The survey was composed of 15 questions voluntarily answered by Spanish gynecology and obstetrics trainees. RESULTS: Compared with a previous survey, a substantial increase in the proportion of Spanish teaching hospitals with an LGTP unit (9/42 vs 47/59) has been detected while doubling the percentage of residents who acknowledge medium to high knowledge on this pathology. The same cannot be said about the handling capacity of vulvodynia registering a great improvement. CONCLUSIONS: Spanish scientific societies, concerned in the quality of LGTP training gained by their residents, have focused on the necessity of LGTP units. Our study confirms the usefulness of this performance in the new continued LGTP education.

Persistent genital arousal disorder: Characterization, etiology, and management.

Facelle TM, Sadeghi-Nejad H, Goldmeier D

J Sex Med. 2012 Nov 15. doi: 10.1111/j.1743-6109.2012.02990.x. [Epub ahead of print]

INTRODUCTION: Persistent genital arousal disorder (PGAD) is a potentially debilitating disorder of unwanted genital sensation and arousal that is generally spontaneous and unrelenting. Since its first description in 2001, many potential etiologies and management strategies have been suggested. AIM: To review the literature on PGAD, identify possible causes of the disorder, and provide approaches to the assessment and treatment of the disorder based on the authors' experience and recent literature. METHODS: PubMed searches through July 2012 were conducted to identify articles relevant to persistent sexual arousal syndrome and PGAD. MAIN OUTCOME MEASURES: Expert opinion was based on review of the medical literature related to this subject matter. RESULTS: PGAD is characterized by persistent sensations of genital arousal in the absence of sexual stimulation or emotion, which are considered unwanted and cause the patient at least moderate distress. The proposed etiologies of PGAD are plentiful and may involve a range of psychologic, pharmacologic, neurologic, and vascular causes. PGAD has been associated with other conditions including overactive bladder and restless leg syndrome. Assessment should include a through history and physical exam and tailored radiologic studies. Treatment should be aimed at reversible causes, whether physiologic or pharmacologic. All patients should be considered for cognitive therapy including mindfulness meditation and acceptance therapy. CONCLUSIONS: PGAD likely represents a range of conditions manifesting in unwanted genital sensations. Successful treatment requires a multidisciplinary approach and consideration of all reversible causes as well as cognitive therapy.

Voiding dysfunction associated with pudendal nerve entrapment.

Possover M, Forman A

Curr Bladder Dysfunct Rep. 2012 Dec;7(4):281-285.

Pudendal nerve entrapment (Alcock canal syndrome) is an uncommon source of chronic pelvic pain, in which the pudendal nerve is entrapped or compressed. Pain is located in the perineal, genital and perianal areas and is worsened by sitting. By simple entrapment of the PN without neurogenic damages, pain is usually isolated. In neurogenic damages to the PN, genito-anal numbness, fecal and/or urinary incontinence can occurred. PNE can be caused by obstetric traumas, scarring due to genitoanal surgeries (prolaps procedures!), accidents and surgical mishaps. Diagnosis is based on anamnesis, clinical examination including vaginal or rectal palpation of the pelvic nerves with selective nerve blockade. Pudendal pain non-systematic mean PNE since other neuropathies may induce pudendal pain.

So sacral radiculopathies (sacral nerves roots S#2-4) are underestimated etiologies frequently responsible for pudendal pain with irradiation in sacral dermatomes, bladder hypersensitivity or in neurogenic lesions, bladder retention.

High-Resolution ultrasound of the pudendal nerve: Normal anatomy.
Tagliafico A, Perez MM, Martinoli C
Muscle Nerve. 2012 Jul 30. doi: 10.1002/mus.23537. [Epub ahead of print]

INTRODUCTION: In this study we aimed to determine whether high-resolution ultrasound (US) can identify the pudendal nerve and its terminal branches. We also attempted to identify the best approach for visualizing these structures. METHODS: Normal anatomy of the pudendal nerve was evaluated in 3 cadavers and 20 healthy volunteers proximally at the level of the ischial spine and distally with low-frequency (2-5-MHZ) and high-frequency (12-7-MHZ and 17-5-MHZ) transducers. Two musculoskeletal radiologists performed the examinations and evaluations. Volunteers were placed in 3 different positions, which allowed different approaches (posterior, medial, and anterior transperineal). A 0-3 scale was used to assess nerve visibility. RESULTS: Visualization of the pudendal nerve at the ischial spine was best when using a medial approach ($P < 0.004$); the terminal branches were seen best with the anterior approach ($P < 0.002$). CONCLUSIONS: High-resolution ultrasound (US) can identify the pudendal nerve and its terminal branches.

Neuromodulation of pelvic visceral pain: Review of the literature and case series of potential novel targets for treatment.
Hunter C, Davé N, Diwan S, Deer T
Pain Pract. 2012 Apr 23. doi: 10.1111/j.1533-2500.2012.00558.x.

Chronic pelvic pain (CPP) is complex and often resistant to treatment. While the exact pathophysiology is unknown, the pain states resultant from conditions such as interstitial cystitis and the like yield patients with a presentation that bears a striking similarity to neuropathic syndromes that are known to respond to neuromodulation. While there has been past success using the sacral region as a target for spinal cord stimulation (SCS) to treat these patients, there remains to be a consensus on the optimal location for lead placement. In this article, the authors discuss the potential etiology of CPP, examine the current literature on lead placement for SCS as a method of treatment, as well as present several cases where novel lead placement was successfully employed.

Mode of delivery and persistence of pelvic girdle syndrome 6 months postpartum.
Bjelland EK, Stuge B, Vangen S, Stray-Pedersen B, Eberhard-Gran M
Am J Obstet Gynecol. 2012 Dec 5. pii: S0002-9378(12)02197-7. doi: 10.1016/j.ajog.2012.12.002. [Epub ahead of print]

OBJECTIVE: We sought to study the association between mode of delivery and persistent pelvic girdle syndrome (PGS) (pain in anterior and bilateral posterior pelvis) 6 months postpartum. STUDY DESIGN: We followed up 10,400 women with singleton deliveries in the Norwegian Mother and Child Cohort Study who reported PGS in pregnancy week 30 (1999 through 2008). Data were obtained by 3 self-administered questionnaires and linked to the Medical Birth Registry of Norway. RESULTS: Planned cesarean section was associated with the presence of severe PGS 6 months postpartum (adjusted odds ratio [OR], 2.3; 95% confidence interval [CI], 1.4-3.9). In women who used crutches during pregnancy, emergency (adjusted OR, 2.0; 95% CI, 1.0-4.0) and planned (adjusted OR, 3.3; 95% CI, 1.9-5.9) cesarean section were each associated with severe PGS. CONCLUSION: The results suggest an increased risk of severe PGS 6 months postpartum in women who underwent a cesarean section vs. women who had an unassisted vaginal delivery.

Pelvic pain: Mechanistically enigmatic, therapeutically challenging.
Puylaert M
Pain Pract. 2013 Jan;13(1):1-2. doi: 10.1111/papr.12019.

No Abstract Available.

Chronic Pain

Epigenetics and the transition from acute to chronic pain.
Buchheit T, Van de Ven T, Shaw A
Pain Med. 2012 Nov;13(11):1474-90. doi: 10.1111/j.1526-4637.2012.01488.x.

OBJECTIVE: The objective of this study was to review the epigenetic modifications involved in the transition from acute to chronic pain and to identify potential targets for the development of novel, individualized pain therapeutics. BACKGROUND: Epigenetics is the study of heritable modifications in gene expression and phenotype that do not require a change in genetic sequence to manifest their effects. Environmental toxins, medications, diet, and psychological stresses can alter epigenetic processes such as DNA methylation, histone acetylation, and RNA interference. As epigenetic modifications potentially play an important role in inflammatory cytokine metabolism, steroid responsiveness, and opioid sensitivity, they are likely key factors in the development of chronic pain. Although our knowledge of the human genetic code and disease-associated polymorphisms has grown significantly in the past decade, we have not yet been able to elucidate the mechanisms that lead to the development of persistent pain after nerve injury or surgery. DESIGN: This is a focused literature review of epigenetic science and its relationship to chronic pain. RESULTS: Significant laboratory and clinical data support the notion that epigenetic modifications are affected by the environment and lead to differential gene expression. Similar to mechanisms involved in the development of cancer, neurodegenerative disease, and inflammatory disorders, the literature endorses an important potential role for epigenetics in chronic pain. CONCLUSIONS: Epigenetic analysis may identify mechanisms critical to the development of chronic pain after injury, and may provide new pathways and target mechanisms for future drug development and individualized medicine.

Is chronic pain a disease?
Cohen M, Quintner J, Buchanan D
Pain Med. 2013 Jan 7. doi: 10.1111/pme.12025

The discovery of neuroplastic phenomena such as central sensitization of nociception has challenged pain theory to evolve, to encompass unpredictable and unlikely chronic pain states, and to cope with the emerging complexity of the brain. Recently, the proposition that chronic pain is a disease in its own right has gained currency, based upon functional and structural changes in the brain constituting a distinctive pathology. Proponents have expanded the theory to identify “eudynia” (“good” pain) and “maldynia” (“bad” pain).

The effects of interdisciplinary team assessment and a rehabilitation program for patients with chronic pain.
Pietilä Holmner E, Fahlström M, Nordström A
Am J Phys Med Rehabil. 2013 Jan;92(1):77-83. doi: 10.1097/PHM.0b013e318278b28e.

OBJECTIVE: The aim of this study was to evaluate the effects of interdisciplinary team assessment and a 4-wk rehabilitation program in chronic pain patients. DESIGN: This was a longitudinal cohort study evaluating interdisciplinary pain rehabilitation measures in a specialist care setting. A total of 93 women (42.2 ± 9.5 yrs) with chronic

musculoskeletal pain (median pain duration, 8 yrs) were evaluated at assessment and at the start and end of the rehabilitation program. Pain intensity measured with a visual analog scale, pain dimensions measured with the Multidimensional Pain Inventory, and anxiety and depression measured with the Hospital Anxiety and Depression Scale were registered. RESULTS: The participants exhibited significantly improved results of pain and pain-related measures. The results were seen both after the short-term intervention in the form of the interdisciplinary assessment and after the 4-wk rehabilitation program. The improvements seen after the assessment were not related to specific interventions, such as change of medication, and therefore seem to be a result of the interdisciplinary assessment concept as such. CONCLUSIONS: Both interdisciplinary assessment and rehabilitation program seem to be effective in chronic pain rehabilitation, at least for women. Further studies are needed to investigate potential sex differences, as well as content and duration for optimal pain rehabilitation programs.

Activity pacing in chronic pain: Concepts, evidence, and future directions.
Nielson WR, Jensen MP, Karsdorp PA, Vlaeyen JW
Clin J Pain. 2012 Dec 14. [Epub ahead of print]

BACKGROUND**:** Activity pacing (AP) is a concept that is central to many chronic pain theories and treatments, yet there remains confusion regarding its definition and effects. OBJECTIVE**:** To review the current knowledge concerning AP and integrate this knowledge in a manner that allows for a clear definition and useful directions for future research. METHODS**:** A narrative review of the major theoretical approaches to AP and of the empirical evidence regarding the effects of AP interventions, followed by an integrative discussion. RESULTS**:** The concept of AP is derived from 2 main traditions: operant and energy conservation. Although there are common elements across these traditions, significant conceptual and practical differences exist, which has led to confusion. Little empirical evidence exists concerning the efficacy of AP as a treatment for chronic pain. DISCUSSION**:** Future research on AP should be based on a clear theoretical foundation, consider the context in which the AP behavior occurs and the type of pacing problem ("underactivity" vs. "overactivity"), and should examine the impact of AP treatment on multiple clinical outcomes. We provide a provisional definition of AP and specific recommendations that we believe will move the field forward.

The effects of graded motor imagery and its components on chronic pain: a systematic review and meta-analysis.
Bowering KJ, O'Connell NE, Tabor A, Catley MJ, Leake HB, Moseley GL, Stanton TR
J Pain. 2013 Jan;14(1):3-13. doi: 10.1016/j.jpain.2012.09.007.

Graded motor imagery (GMI) is becoming increasingly used in the treatment of chronic pain conditions. The objective of this systematic review was to synthesize all evidence concerning the effects of GMI and its constituent components on chronic pain. Systematic searches were conducted in 10 electronic databases. All randomized controlled trials (RCTs) of GMI, left/right judgment training, motor imagery, and mirror therapy used as a treatment for chronic pain were included. Methodological quality was assessed using the Cochrane risk of bias tool. Six RCTs met our inclusion criteria, and the methodological quality was generally low. No effect was seen for left/right judgment training, and conflicting results were found for motor imagery used as stand-alone techniques, but positive effects were observed for both mirror therapy and GMI. A meta-analysis of GMI versus usual physiotherapy care favored GMI in reducing pain (2 studies, n = 63; effect size, 1.06 [95% confidence interval, .41, 1.71]; heterogeneity, I(2) = 15%). Our results suggest that GMI and mirror therapy alone may be effective, although this conclusion is based on limited evidence. Further rigorous studies are needed to investigate the effects of GMI and its components on a wider chronic pain population. PERSPECTIVE: This systematic review synthesizes the evidence for GMI and its constituent components on chronic pain. This review may assist clinicians in making evidence-based decisions on managing patients with chronic pain conditions.

Which skills are associated with residents' sense of preparedness to manage chronic pain?
Fox AD, Kunins HV, Starrels JL
J Opioid Manag. 2012 Sep-Oct;8(5):328-36. doi: 10.5055/jom.2012.0132.

OBJECTIVE: To identify gaps in residents' confidence and knowledge in managing chronic nonmalignant pain (CNMP) and to explore whether specific skills or pain knowledge was associated with global preparedness to manage CNMP. DESIGN: Cross-sectional web-based survey. SETTING AND PARTICIPANTS: Internal medicine residents in Bronx, NY. MAIN OUTCOME MEASURES: The authors assessed the following: 1) confidence in skills within the following four content areas: physical examination, diagnosis, treatment, and safer opioid prescribing; 2) pain-related knowledge on a 16-item scale; and 3) global preparedness to manage CNMP (agreement with, "I feel prepared to manage CNMP"). Gaps in confidence were skills in which fewer than 50 percent reported confidence. Gaps in knowledge were items in which fewer than 50 percent answered correctly. Using logistic regression, the authors examined whether skills or knowledge was associated with global preparedness. RESULTS**:** Of 145 residents, 92 (63 percent) responded. Gaps in confidence included diagnosing fibromyalgia, performing corticosteroid injections, and using pain medication agreements. Gaps in knowledge included pharmacotherapy for neuropathic pain and interpreting urine drug test results. Twenty-four residents (26 percent) felt globally prepared to manage CNMP. Confidence using pain medication agreements (adjusted odds ratio [AOR], 5.99; 95% confidence interval [CI], 2.02-17.75), prescribing long-acting opioids (AOR, 5.85; 95% CI, 2.00-17.18), and performing corticosteroid injection of the knee (AOR, 5.76; 95% CI, 1.16-28.60]) were strongly associated with global preparedness. CONCLUSIONS: Few internal medicine residents felt prepared to manage CNMP. Our findings suggest that educational interventions to improve residents' preparedness to manage CNMP should target complex pain syndromes (eg, fibromyalgia and neuropathic pain), safer opioid prescribing practices, and alternatives to opioid analgesics.

Neurophysiological assessment of painful neuropathies.
Barraza-Sandoval G, Casanova-Mollá J, Valls-Solé J
Expert Rev Neurother. 2012 Nov;12(11):1297-310. doi: 10.1586/ern.12.93.

Nociceptive inputs reach the CNS by means of small myelinated and unmyelinated fibers. Owing to this, conventional nerve conduction studies and electromyography are less likely to demonstrate abnormalities in neuropathies affecting nociceptive fibers than in those involving large myelinated fibers. Therefore, to characterize painful neuropathies, clinicians evaluate the features of the lesion that cause pain rather than the feeling of pain itself. Clinical neurophysiological assessment of painful neuropathies still relies on conventional nerve conduction studies but slightly more sophisticated techniques bring more specific information. These are the nociceptive-evoked potentials, microneurography or autonomic nervous system functional tests. Neurophysiological techniques can also add information to quantitative sensory testing by recording autonomic responses such as the sudomotor skin response or the voluntary reaction. Functional magnetic resonance should also be considered as a neurophysiological technique, which allows for mapping the areas of the brain involved in nociceptive sensation and pain control.

Redesigning delivery of opioids to optimize pain management, improve outcomes, and contain costs.
Cahana A, Dansie EJ, Theodore BR, Wilson HD, Turk DC
Pain Med. 2012 Dec 28. doi: 10.1111/pme.12013. [Epub ahead of print]

INTRODUCTION: Chronic pain is a public health concern, and in the last decade, there has been a dramatic increase in the use and abuse of prescription opioids for chronic non-cancer pain. METHODS: We present an overview of a five-component model of pain management implemented at the University of Washington Division of Pain Medicine designed to facilitate recent state guidelines to reduce the risks associated with long-term use of prescription opioids. RESULTS: Central to the model described are guidelines for best clinical practice, a collaborative care approach, telehealth solutions, comprehensive prescription-monitoring, and measurement-based care. DISCUSSION: The model presented is a patient-centered, efficient, and cost-effective approach to the management of chronic pain.

An evaluation of the prescription of opioids for chronic nonmalignant pain by Australian general practitioners.
Holliday S, Magin P, Dunbabin J, Oldmeadow C, Henry JM, Lintzeris N, Attia J, Goode S, Dunlop A
Pain Med. 2012 Dec 28. doi: 10.1111/j.1526-4637.2012.01527.x. [Epub ahead of print]

OBJECTIVE: Our objective was to evaluate the quality of opioid analgesia prescribing in chronic nonmalignant pain (CNMP) by general practitioners (GPs, family physicians). DESIGN: An anonymous, cross-sectional questionnaire-based survey. SETTING: The setting was five Australian divisions of general practice (geographically based associations of GPs). METHODS: A questionnaire was mailed to all division members. Outcome measures were adherence to individual recommendations of locally derived CNMP practice guidelines. RESULTS: We received 404 responses (response rate 23.3%). In the previous fortnight, GPs prescribed long-term continuous opioids for CNMP for a median of 4 and a mean of 7.1 (±8.7) patients with CNMP. Guideline concordance (GLC) was poor, with no GP always compliant with all guideline items, and only 31% GPs usually employing most items. GLC was highest for the avoidance of high dosages or fast-acting formulations. It was lowest for strategies minimizing individual and public health harms, such as the initiation of opioids on a time-limited trial basis, use of contracts, and the preclusion or management of aberrant behaviors. GLC was positively associated with relevant training or qualifications, registration with the Australian Prescription Drug Monitoring Programme, being an opioid substitution therapy prescriber, and female gender. CONCLUSIONS: In this study, long-term opioids were frequently initiated for CNMP without a quality use-of-medicine approach. Potential sequelae are inadequate treatment of pain and escalating opioid-related harms. These data suggest a need for improved resourcing and training in opioid management across pain and addictions.

Single versus composite measures of pain intensity: Relative sensitivity for detecting treatment effects.
Jensen MP, Hu X, Potts SL, Gould EM
Pain. 2012 Dec 28. doi: 10.1016/j.pain.2012.12.017

Assay sensitivity remains a significant issue in pain clinical trials. One possible method for increasing assay sensitivity for detecting changes in pain intensity is to increase the reliability of pain intensity assessment by increasing the number of intensity ratings obtained, and combining these ratings into composite scores. The current study performed secondary analyses from a published clinical trial to test this possibility. The reliability and assay sensitivity pain intensity scores made up of one to nine 24-hour pain intensity recall ratings were compared. Although the reliability of the outcome measures improved as the number of items increased, this increase in reliability was not associated with an increase in assay sensitivity. A single 24-hour recall rating was about as valid (sensitive) for detecting treatment effects as composite scores made up of two to nine different ratings. If this finding replicates in other pain populations, it has significant implications for the design and conduct of pain clinical trials. Specifically, it suggests the possibility that assessment burden (and associated costs and problems related to missing data) might be greatly reduced by specifying a single recall rating as the primary outcome variable. Research is needed to explore this possibility further.

The predictive value of attentional bias towards pain-related information in chronic pain patients: A diary study.
Van Ryckeghem DML, Crombez G, Goubert L, De Houwer J, Onraedt T, Van Damme S
Pain. 2012 Dec 28. doi: 10.1016/j.pain.2012.12.008

Theoretical accounts of chronic pain hypothesize that attentional bias towards pain-related information is a maintaining or exacerbating factor, fuelling further pain, disability and distress. However, empirical research testing this idea is currently lacking. In the present study, we investigated whether attentional bias towards pain-related information predicts daily pain-related outcomes in a sample of chronic pain patients (N = 69; M_{age} = 49.64; 46 females). During an initial laboratory session attentional bias to pain-related information was assessed using a modified spatial cueing task. In advance, patients completed a number of self-report measures assessing current pain intensity, current disability, and pain duration. Subsequently, daily pain outcomes (self-reported pain severity, disability, avoidance behaviour and

distractibility) were measured for two weeks by means of an electronic diary. Results indicated that, although an attentional bias towards pain-related information was associated with the current level of disability and pain severity, it had no additional value above control variables in predicting daily pain severity, avoidance, distractibility and disability. Attentional bias towards pain-related information did however moderate the relationship between daily pain severity and both daily disability and distractibility, indicating that particularly in those patients with a strong attentional bias, increases in pain were associated with increased disability and distractibility. The use of interventions that diminish attentional bias may therefore be helpful to reduce daily disability and the level of distraction from current tasks despite the presence of pain in chronic pain patients.

The relationship between PTSD and chronic pain: Mediating role of coping strategies and depression.
Morasco BJ, Lovejoy TI, Lu M, Turk DC, Lewis L, Dobscha SK
Pain. 11 Jan 2013. doi: 10.1016/j.pain.2013.01.001

People with chronic pain and comorbid posttraumatic stress disorder (PTSD) report more severe pain and poorer quality of life than those with chronic pain alone. This study evaluated the extent to which associations between PTSD and chronic pain interference and severity are mediated by pain-related coping strategies and depressive symptoms. Veterans with chronic pain were divided into two groups, those with (n=65) and those without (n=136) concurrent PTSD. All participants completed measures of pain severity, interference, emotional functioning, and coping strategies. Those with current PTSD reported significantly greater pain severity and pain interference, had more symptoms of depression, and were more likely to meet diagnostic criteria for a current alcohol or substance use disorder (all p-values $\leqslant 0.01$). Participants with PTSD reported more use of several coping strategies, including guarding, resting, relaxation, exercise/stretching, and coping self-statements. Illness-focused pain coping (i.e., guarding, resting, and asking for assistance) and depressive symptoms jointly mediated the relationship between PTSD and both pain interference (total indirect effect = 0.194, $p < 0.001$) and pain severity (total indirect effect = 0.153, $p = 0.004$). Illness-focused pain coping also evidenced specific mediating effects, independent of depression. In summary, specific pain coping strategies and depressive symptoms partially mediated the relationship between PTSD and both pain interference and severity. Future research should examine whether changes in types of coping strategies following targeted treatments predict improvements in pain-related function for chronic pain patients with concurrent PTSD.

Suicidality associated with anti-epileptic drugs: implications for the treatment of neuropathic pain and fibromyalgia.
Pereira A, Gitlin MJ, Gross RA, Posner K, Dworkin RH
Pain. 11 Jan 2013. doi: 10.1016/j.pain.2012.12.024

No Abstract Available.

Vulvovaginal Disorders

An overview of chronic vaginal atrophy and options for symptom management.
Woods NF
Nurs Womens Health. 2012 Dec;16(6):482-94. doi: 10.1111/j.1751-486X.2012.01776.x.

During the menopausal transition and after menopause, up to 45 percent of women will develop vaginal atrophy as a consequence of decreased levels of circulating estrogen. Symptoms include vaginal dryness, itching, soreness, bleeding, increased susceptibility to infection and pain with sexual intercourse. Treatments are often underused because of patient and clinician lack of knowledge of available treatments, embarrassment about initiating a discussion of symptoms and reluctance to initiate hormonal therapy. Methods of symptom management include self-care with over-

the-counter agents and prescription treatment with various forms of localized estrogen. Clinicians should consider each woman's unique situation and health history before recommending a management strategy.

Fluconazole-resistant Candida albicans vulvovaginitis.
Marchaim D, Lemanek L, Bheemreddy S, Kaye KS, Sobel JD
Obstet Gynecol. 2012 Dec;120(6):1407-14. doi: 10.1097/AOG.0b013e31827307b2.

OBJECTIVE: As a result of high recurrence rates of Candida albicans vaginitis, successful suppressive fluconazole is widely used, and drug resistance is considered rare. We report increased occurrence of secondary fluconazole resistance, analysis of risk factors thereof, and describe management of fluconazole-refractory vaginitis. METHODS: Patients referred to the Vaginitis Clinic at Wayne State University with clinically refractory fluconazole-resistant (minimum inhibitory concentration [MIC] 2 micrograms/mL or greater) C albicans vaginitis from 2000 to 2010 were enrolled. Patients completed a questionnaire pertaining to demographics, comorbidities, behavioral characteristics, exposure to antimicrobials and antifungals, fluconazole consumption in defined daily doses in the previous 6 months, management received, and outcomes. With patients not located, data were extracted from charts. Susceptibilities to antifungals were determined by broth microdilution. RESULTS: Twenty-five women with fluconazole-resistant recurrent C albicans vaginitis were identified, and 16 returned filled questionnaires. Study cohort consisted mainly of married, insured white women with more than 12 years of formal education and average or above average socioeconomic status. Median fluconazole MIC was 8 micrograms/mL (range 2-128 micrograms/mL). Risk factors for mycologic failure included increased fluconazole consumption (P=.03) with 16 of 25 women exposed to low-dose weekly fluconazole maintenance therapy. All patients were clinically controlled successfully, although treatment was difficult and often prolonged. CONCLUSION: Fluconazole-resistant C albicans vaginitis was previously considered rare. We report 25 cases over an 11-year period, indicating an emerging problem. All patients had fluconazole consumption in the previous 6 months. Management of fluconazole refractory disease is extremely difficult with limited options, and new therapeutic modalities are needed.

Rapid identification of drug resistant Candida species causing recurrent vulvovaginal candidiasis.
Diba K, Namaki A, Ayatolahi H, Hanifian H
Med Mycol J. 2012;53(3):193-8.

Some yeast agents including Candida albicans, Candida tropicalis and Candida glabrata have a role in recurrent vulvovaginal candidiasis. We studied the frequency of both common and recurrent vulvovaginal candidiasis in symptomatic cases which were referred to Urmia Medical Sciences University related gynecology clinics using morphologic and molecular methods. The aim of this study was the identification of Candida species isolated from recurrent vulvovaginal candidiasis cases using a rapid and reliable molecular method. Vaginal swabs obtained from each case, were cultured on differential media including cornmeal agar and CHROM agar Candida. After 48 hours at 37°Ç, the cultures were studied for growth characteristics and color production respectively. All isolates were identified using the molecular method of PCR - restriction fragment length polymorphism. Among all clinical specimens, we detected 19 (16 %) non fungal agents, 87 (82.1 %) yeasts and 2 (1.9 %) multiple infections. The yeast isolates identified morphologically included Candida albicans (n = 62), Candida glabrata (n = 9), Candida tropicalis (n = 8), Candida parapsilosis (n = 8) and Candida guilliermondii and Candida krusei (n = 1 each). We also obtained very similar results for Candida albicans, Candida glabrata and Candida tropicalis as the most common clinical isolates, by using PCR - Restriction Fragment Length Polymorphism. Use of two differential methods, morphologic and molecular, enabled us to identify most medically important Candida species which particularly cause recurrent vulvovaginal candidiasis.

Question: In females being treated with antibiotics, is probiotic use effective in reducing the incidence of vulvovaginal candidiasis?
Ainsworth J, Nail M, Fox A
J Okla State Med Assoc. 2012 Sep;105(9):349-50.

No Abstract Available.

Weekly fluconazole therapy for recurrent vulvovaginal candidiasis: a systematic review and meta-analysis.
Rosa MI, Silva BR, Pires PS, Silva FR, Silva NC, Silva FR, Souza SL, Madeira K, Panatto AP, Medeiros LR
Eur J Obstet Gynecol Reprod Biol. 2012 Dec 29. doi: 10.1016/j.ejogrb.2012.12.001. [Epub ahead of print]

OBJECTIVE: To investigate the efficacy, compared to placebo, of fluconazole 150mg weekly, given for six months as prophylaxis against recurrent vulvovaginal candidiasis (RVVC). STUDY DESIGN: A quantitative systematic review was performed, and randomized controlled trials were included. We conducted searches at Medline, EMBASE, Lilacs, Cochrane Library and ICI Web of Science from 1980 to March 2012. We used the odds ratio (OR) with confidence intervals (CI) of 95% using a random effects model of Mantel-Haenszel. The software used was Review Manager version 5.0. RESULTS: Through the search strategies we identified 249 articles, of which only two were part of the meta-analysis. Fluconazole was more effective than placebo in reducing symptomatic episodes of VVC, immediately after treatment (OR 0.10, 95% CI 0.03-0.34), 3 months after treatment (OR 0.23, 95% CI 0.07-0.74) and 6 months after treatment (OR 0.39, 95% CI 0.24-0.64). CONCLUSION: Weekly treatment with fluconazole (150mg) for six months is effective against RVVC.

Efficacy and tolerability of fitostimoline (vaginal cream, ovules, and vaginal washing) and of benzydamine hydrochloride (tantum rosa vaginal cream and vaginal washing) in the topical treatment of symptoms of bacterial vaginosis.
Boselli F, Petrella E, Campedelli A, Muzi M, Rullo V, Ascione L, Papa R, Saponati G
ISRN Obstet Gynecol. 2012;2012:183403. doi: 10.5402/2012/183403.

Two hundred and 91 patients showing signs and symptoms of bacterial vaginosis (BV) were randomized to receive topical treatment with Fitostimoline (vaginal cream and vaginal ovules + vaginal washing) or benzydamine hydrochloride (vaginal cream + vaginal washing) for 7 days. Signs (leucorrhoea, erythema, oedema, and erosion) and symptoms (burning, pain, itching, vaginal dryness, dyspareunia, and dysuria) (scored 0-3) were evaluated at baseline and at the end of treatment; the total symptoms score (TSS) was also calculated. In 125 patients, a bacterial vaginosis was confirmed by vaginal swab test. The primary efficacy variable analysis, that is, the percentage of patients with therapeutic success (almost complete disappearance of signs and symptoms), demonstrated that Fitostimoline ovules and vaginal cream were therapeutically equivalent and that pooled Fitostimoline treatment was not inferior to benzydamine hydrochloride. All the treatments were well tolerated, with only minor local adverse events infrequently reported. The results of this study confirmed that gynaecological Fitostimoline is a safe and effective topical treatment for BV.

Altered CD16 expression on vaginal neutrophils from women with vaginitis.
Beghini J, Giraldo PC, Riboldi R, Amaral RL, Eleutério J Jr, Witkin SS, Guimarães F
Eur J Obstet Gynecol Reprod Biol. 2012 Dec 20. doi: 10.1016/j.ejogrb.2012.11.008. [Epub ahead of print]

OBJECTIVE: Reduced CD16 expression is associated with neutrophil apoptosis. This study aimed to compare CD16 expression on neutrophils in the vagina from women with normal bacterial flora and with vaginitis. STUDY DESIGN: Vaginal lavages were sampled from volunteers diagnosed with bacterial vaginosis (BV, n=34), vulvovaginal candidiasis (VC, n=43), BV plus VC (BV+VC, n=14), and normal flora (NF, n=51). Neutrophils were identified by expression of CD15, CD16 and CD24 surface markers as assessed by flow cytometry. RESULTS: CD16 expression was elevated in neutrophils

from women with vaginitis (BV p<0.0001; VC p=0.01; BV+VC p=0.0027) as compared to women with NF. CONCLUSION: The reduction in CD16 down-regulation is consistent with prolonged neutrophil viability and activity in the vagina of women with vaginitis. This may contribute to greater microbial clearance and, conversely, with inflammation-associated pathology.

Association of autoimmune diseases with lichen sclerosus in 532 male and female patients.
Kreuter A, Kryvosheyeva Y, Terras S, Moritz R, Möllenhoff K, Altmeyer P, Scola N, Gambichler T
Acta Derm Venereol. 2012 Dec 6. doi: 10.2340/00015555-1512. [Epub ahead of print]

Lichen sclerosus is a relatively common chronic inflammatory skin disease that predominantly affects the anogenital area. Accumulating evidence indicates that lichen sclerosus in women may be associated with other autoimmune disease, whereas this association seems to lack in male patients. We retrospectively evaluated the prevalence of autoimmune diseases and serological parameters indicative for autoimmunity in male and female patients with lichen sclerosus. Of the 532 patients (396 women, 136 men; 500 adults, 32 children; mean age: 49 years; range 1-89 years; female:male ratio 3:1), 452 (85%) had genital and 80 (15%) had extragenital disease. In women, lichen sclerosus was significantly more often associated with at least one autoimmune disease as compared to men (odds ratio [OR] 4.3, 95% confidence interval [CI] 1.9-9.6; p < 0.0001). Moreover, female patients with lichen sclerosus had sinificantly more often associated autoimmune thyroid diseases (OR 4.7, 95% CI 1.8-11.9; p < 0.0002), antithyroid-antibodies (OR 2.7, 95% CI 1.1-6.5; p = 0.023), and elevated autoantibodies (OR 4.1, 95% CI 1.9-9.3; p < 0.0001) as compared to male patients. This observation is suggestive for a different pathogenetic background in male and female patients.

Quality of life in Dutch women with lichen sclerosus.
Lansdorp CA, van den Hondel KE, Korfage IJ, van Gestel MJ, van der Meijden WI
Br J Dermatol. 2012 Dec 18. doi: 10.1111/bjd.12137. [Epub ahead of print]

BACKGROUND: Lichen sclerosus (LS) is a chronic inflammatory skin disease. Earlier studies have shown an impaired health-related quality of life (HRQoL), but more extensive research including generic questionnaires has not been reported. OBJECTIVES: In this cross-sectional study we investigate the HRQoL of a sample of Dutch women with LS. Resulting HRQoL data will be compared with that available from other skin diseases and the general Dutch population. Additionally, we explore factors possibly influencing the HRQoL. METHODS: Female members of the Dutch LS Foundation and Support Group(1) electronically filled out three questionnaires; the Skindex-29, the SF-12 and the EQ-5D VAS. We distinguished groups of Skindex-29 scores with "little" (score 0-24), "mild" (25-31), "moderate" (32-43) and "severe" (44-100) impact on HRQoL. We compared differences using the Mann-Whitney U-test and the Kruskal Wallis Test, and correlations using Spearman's rank correlation coefficient. RESULTS: 262 women with LS were included. The average diagnostic delay was 4.9 (SD = 7.1) years. Patients had a mean total Skindex-29 score of 38.4 (0-100, SD=17.2). Domain scores for symptoms, emotions and functioning were 48.8 (SD=19.0), 38.2 (SD=20.2) and 33.6 (SD=19.3), respectively. The SF-12 showed an average PCS-12 and MCS-12 score of 47.7 and 48.5 respectively. For the average Dutch population these scores were 49.3 and 52.3. The average EQ-5D VAS score was 74.1 (SD=15.4). CONCLUSIONS: There is a considerable diagnostic delay in Dutch female patients with LS. The Skindex-29 domain scores showed a moderately impaired HRQoL. Female patients with LS reported a lower generic HRQoL than the average female Dutch population.

A therapeutic approach for female, relapsing genital lichen sclerosus: a single-center study.
Patsatsi A, Kyriakou A, Vavilis D, Mantas A, Patsialas C, Sotiriadis D
J Dermatolog Treat. 2012 Nov 19. [Epub ahead of print]

OBJECTIVE: To assess the efficacy of methylprednisolone aceponate 0.1% (MPA) in female genital lichen sclerosus (GLS) and efficacy of MPA, tacrolimus or emollient for prevention of flares. METHODS: A single-center, retrospective study

was conducted. At baseline, female patients with relapsing GLS (n=46) were treated with MPA 0.1% applied once daily for 8 weeks. Visual Analog Scale (VAS) score for vulvar pruritus and Investigator's Global Assessment (IGA) score were recorded at baseline, week-8 and 20. At week-8, patients responsive to treatment (n=38), were further treated with MPA 0.1% twice weekly (n=15), tacrolimus once daily (n=13) or topical emollient once daily (n=10), as maintenance therapy until week-20. RESULTS: Both VAS and IGA median score was significantly decreased from baseline to week-8 (p=0.000). At week-20 both median VAS and IGA score differed significantly between 1) patients treated with emollient and patients treated with MPA 0.1% (p=0.000), and 2) patients treated with emollient and patients treated with tacrolimus (p=0.000); patients treated with MPA 0.1% presented no significant difference in either median VAS score (p=0.032) or median IGA score (p=0.636) at week-20 compared to patients treated with tacrolimus. CONCLUSIONS: MPA is effective in relapsing female GLS. MPA and tacrolimus have equal efficacy in preventing relapses.

Eosinophilic spongiosis in vulvar lichen sclerosus.
Kiyohara T, Satoh S, Kumakiri M
J Dermatol. 2012 Dec 6. doi: 10.1111/1346-8138.12044. [Epub ahead of print]

No Abstract Available.

Langerhans cell histiocytosis associated with lichen sclerosus of the vulva: case report and review of the literature.
Chang JC, Blake DG, Leung BV, Plaza JA
J Cutan Pathol. 2012 Nov 20. doi: 10.1111/cup.12051. [Epub ahead of print]

Langerhans cell histiocytosis (LCH) is characterized by a clonal proliferation of bone marrow-derived Langerhans cells. While cutaneous involvement is relatively common, LCH restricted to the vulvar area is a rare phenomenon and can occur in different clinical settings. Occasionally, vulvar LCH heralds subsequent multi-organ involvement with an aggressive clinical course. Even cases of LCH isolated to the vulvar area can present with local recurrences despite excision and radiation. We present a case of a 68-year-old female with a 1-month history of pruritic lesions on her vulva. Physical examination showed whitish plaques with scattered nodular areas on the labia majora. A vulvar biopsy showed a background of lichen sclerosus (LS) with foci of oval to polygonal cells with moderately abundant eosinophilic cytoplasm and folded nuclei showing frequent nuclear grooves. Immunohistochemical staining showed that the cells were positive for CD1a and S-100, confirming the diagnosis of LCH. On further workup, there was no evidence of disseminated disease involving other organs. While vulvar LCH is uncommonly seen, and with only one previous case report in the literature associated in the setting of lichen sclerosus, this case illustrates the importance of recognizing this condition and ensuring proper clinical follow-up to rule out a systemic involvement.

Inverse psoriasis involving genital skin folds: Successful therapy with dapsone.
Guglielmetti A, Conlledo R, Bedoya J, Ianiszewski F, Correa J
Dermatol Ther (Heidelb). 2012 Dec;2(1):15.

INTRODUCTION: Inverse psoriasis is a rare form of psoriasis that affects between 3% and 7% of the patients with psoriasis. It can comprise genital skin folds as part of genital psoriasis, and it is one of the most commonly seen dermatoses of this area. There are few evidence-based studies about the treatment of intertriginous psoriasis involving genital skin folds. CASE PRESENTATION: The authors present a 42-year-old female patient with erythematous plaques in the vulva, groin, and perianal region. The patient had previously received a broad range of topical and systemic therapies that had to be discontinued due to ineffectiveness or side effects. She was treated with 100 mg dapsone daily for 10 months, showing a significant improvement of her cutaneous and mucous lesions. Complete clearance of psoriatic lesions was observed after 4 weeks of treatment. She has remained in remission for up to 2 years, using only topical therapy with tacrolimus 0.1% and calcipotriol. DISCUSSION: Genital psoriasis is a skin disease that causes great discomfort. It is important to include examination of the genital region and to adopt this conduct in daily clinical

practice. Research in this field is still poor, making no discrimination between flexural and genital psoriasis, and is based on case series and expert opinion; therefore, empirical recommendations for the treatment of genital psoriasis remain. Dapsone has been shown to be an effective and convenient alternative for the treatment of inverse psoriasis in genital skin folds, which can provide effective control of the disease. Further studies are required to determine the efficacy and safety of current therapies, and to decide whether dapsone therapy should be considered in the management of this form of psoriasis when topical and other systemic agents are not effective.

Postoperative sexual concerns and functioning in patients who underwent lysis of vulvovaginal adhesions.
Suzuki V, Haefner HK, Piper CK, O'Gara C, Reed BD
J Low Genit Tract Dis. 2013 Jan;17(1):33-7. doi: 10.1097/LGT.0b013e318252d347.

OBJECTIVE: This study aimed to determine satisfaction and functioning before and after surgery among women with lichen planus, who have undergone lysis of vulvovaginal adhesions, and to compare their sexual functioning with those of women without this disorder. MATERIALS AND METHODS: The study was approved by the University of Michigan Internal Review Board. A retrospective self-administered survey was completed by 22 women (50-76 years). Eleven women who had undergone surgery to release vulvovaginal adhesions from lichen planus answered a mailed, 75-item questionnaire about health, sexual functioning (using the Female Sexual Function Index), and satisfaction with surgical outcomes 6 months to 6 years after their lysis of vulvovaginal adhesions followed by long-term vaginal dilation. They were compared with 11 age-matched normal controls. We used descriptive statistics such as mean and SDs to describe the population and χ and t tests to determine significant differences between groups. RESULTS: Surgery in women with lichen planus scarring allowed intercourse in 55% and decreased urination difficulties in 75%. Of the patients, 91% stated they were happy with the surgery and would recommend it to others. However, sexual difficulties may persist even after surgery. Approximately 50% of the patients continue to fear pain. There continues to be differences between cases and controls in sexual discomfort and sexual satisfaction. CONCLUSIONS: After surgery for lichen planus, women tend to be more likely to have intercourse, to have less urinary symptoms or infections, and to have fewer genital symptoms. However, for some, sexual difficulties persisted. It may be wise to consider sexual counseling for this population. Nevertheless, most of the patients stated that they were happy with the surgery and would recommend it to others.

Pathways of vulvar intraepithelial neoplasia and squamous cell carcinoma.
Del Pino M, Rodriguez-Carunchio L, Ordi J
Histopathology. 2013 Jan;62(1):161-75. doi: 10.1111/his.12034.

Vulvar squamous cell carcinoma (VSCC) accounts for >90% of the malignant tumours of the vulva. Most VSCCs originate in intraepithelial lesions, named vulvar intraepithelial neoplasia (VIN), that precede the development of VSCC by a variable period of time. Strong evidence has accumulated showing that there are two different aetiopathogenic pathways for the development of VSCC and VIN, one associated with infection by human papillomavirus (HPV), and a second independent of HPV infection. These two different types of VSCC have different epidemiological, pathological and clinical characteristics, and should therefore be considered as two separate entities. Histologically, HPV-associated VSCCs are of the basaloid or warty type, and arise from VIN of the usual type. Inactivation of p53 and the retinoblastoma tumour suppressor gene product by the viral gene products E6 and E7 is involved in the process of malignant transformation. HPV-independent VSCCs are histologically keratinizing, are associated with differentiated VIN and lichen sclerosus, and frequently show mutations of p53. p16(INK4a) and p53 immunostaining can be useful for classifying VSCC into HPV-associated or HPV-independent. Although large, multicentre studies are needed to definitively assess the involvement of HPV in the prognosis of VSCC, most studies have not found clear differences in survival between HPV-associated and HPV-independent tumours.

Quality of life and sexuality of patients after treatment for gynaecological malignancies: results of a prospective study in 55 patients.

Pilger A, Richter R, Fotopoulou C, Beteta C, Klapp C, Sehouli J

Anticancer Res. 2012 Nov;32(11):5045-9.

AIM: To assess the sexuality and quality of life (QoL) of women with gynaecological malignancies after multimodal therapy. MATERIALS AND METHODS: This is a prospective analysis of the sexual status among women after treatment for gynaecological malignancies. Validated questionnaires-female sexual function index (FSFI-d), a semi-structured questionnaire and the quality of life score SF12, were applied. RESULTS: Overall, 55 patients (median age=61, range=22-74 years) were enrolled. The cancer diagnoses were 54% ovarian, 26% breast, 13% cervical, 6% vulvar and 2% endometrial cancer. Twenty patients (55.6%) claimed experiencing changes in their sexuality after cancer treatment. The main reasons for this impairment were distorsion of their self image (45%; n=9), dry vaginal mucosa (25%; n=5), fear of physical harm (20%; n=4) and pain during sexual intercourse (20%; n=4). Forty percent of the patients gave no information about their sexuality after cancer therapy. Patients with cervical, endometrial or vulvar cancer had significantly higher changes in their sexuality compared to patients with ovarian cancer even after adjusting for age, recurrence rate and partnership status. The evaluation of SF12 revealed significantly higher psychological functional scores with increasing age. Patients who reported changes of their sexuality were also shown to have a lower overall SF12 score. CONCLUSION: Evaluation of sexuality and self image perception after cancer treatment is an unmet need and needs to be addressed in women with gynaecological malignancies. Further studies are warranted to assess the influence of the various types of cancer therapies in regard to their effect on sexuality and quality of life.

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.