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Vulvodynia / Vulvovaginal Pain

Economic burden and quality of life of vulvodynia in the United States.

Xie Y, Shi L, Xiong X, Wu E, Veasley C, Dade C

Curr Med Res Opin. 2012 Feb 23. [Epub ahead of print]

OBJECTIVE: To explore the economic burden and quality of life of vulvodynia in the United States. METHODS: We conducted a web-based survey from 2009 to 2010. Patients who responded to the advertisement of National Vulvodynia Association completed the survey every month recording their own costs and their employers' payments related to vulvodynia in the past month. A total of 302 patients entered data for at least one month and among them, 97 patients had completed data for six months. We used multiple imputation to generate values for unobserved cost components. For insurance payments, we also extracted the average insurance payments for direct health care service related to vulvodynia from a commercial insurance database. The total costs were disaggregated into direct health care costs, direct non-health care costs and indirect costs. We also assessed patients' quality of life by using Euro QOL 5 dimensions (EQ-5D) in a follow-up survey. RESULTS: The total costs in six months were $8862.40 per patient, of which $6043.34 (68.19%) was direct health care costs, $553.81 (6.25%) was direct non-health care costs and $2265.25 (25.56%) was indirect costs. Based on the reported prevalence range of 3% to 7% in the U.S., our analysis yielded an annual national burden ranging from $31 billion to $72 billion in the United States. Yet the estimate should be viewed with caution as our study sample was a non-probability sample. The average EQ-5D score was 0.74±0.19 among vulvodynia patients. CONCLUSION: Vulvodynia is associated with a huge economic burden to both individuals and the society. It is also related to a relatively low quality of life.

Diffuse noxious inhibitory control function in women with provoked vestibulodynia.

Sutton KS, Pukall CF, Chamberlain S

Clin J Pain. 2011 Dec 30. [Epub ahead of print]

OBJECTIVES: The objective of the study was to assess diffuse noxious inhibitory control (DNIC) function in women with provoked vestibulodynia (PVD) compared with healthy controls through the use of 2 different methodologies. Furthermore, the study aimed to assess whether pain characteristics correlate with DNIC in women with PVD. METHODS: Twenty-three healthy control women and 23 women diagnosed with PVD by the study gynecologist participated in the study. To assess DNIC, heat pain tolerance, determined through an ascending method of limits and temporal summation of thermal pain were used as test stimuli and a cold water bath was used as the conditioning

stimulus. Participants reported on pain characteristics as potential correlates with DNIC function. RESULTS: No significant group differences were found in the number of DNIC responders per group when using heat pain tolerance or temporal summation procedures to examine DNIC. The magnitude of the DNIC response was examined for the overall groups and for positive DNIC responders only. When all participants were included in the analyses with the heat pain tolerance procedure, women with PVD displayed a higher magnitude of DNIC responding. Correlations between pain variables and DNIC responding and magnitude were nonsignificant. DISCUSSION: Results support previous findings of intact DNIC function in women with PVD, using both an ascending method of limits and a temporal summation paradigm. Pain-related variables were not correlated with DNIC function in women with PVD, perhaps this unexpected finding is due to the possibility that central processes other than DNIC, such as descending facilitation, provoke or maintain this chronic pain condition.

Provoked vestibulodynia-Medical factors and comorbidity associated with treatment outcome.
Heddini U, Bohm-Starke N, Nilsson KW, Johannesson U
J Sex Med. 2012 Feb 29. doi: 10.1111/j.1743-6109.2012.02665.x. [Epub ahead of print]

INTRODUCTION: Provoked vestibulodynia (PVD) is the most common cause of dyspareunia in young women. The etiology is unclear, and there is little knowledge of how to predict treatment outcome. AIM: The aim of this study was to identify medical factors associated with treatment outcome and coital pain in women with PVD. METHODS: Seventy women previously treated for PVD at a vulvar open care unit completed questionnaires and a quantitative sensory testing session. MAIN OUTCOME MEASURES: Concomitant bodily pain and treatment outcome were surveyed using a study specific questionnaire. Coital pain was rated on a visual analog scale (VAS), range 0-100. Psychometric screening was carried out using the Hospital Anxiety and Depression Scale. Pressure pain thresholds on the arm, leg, and in the vestibulum were measured using pressure algometers. RESULTS: Major improvement/complete recovery was more likely in PVD patients with a maximum of one other concomitant pain disorder compared with patients with four or more (odds ratio = 7.8, confidence interval: 1.2-49.4, P = 0.03). In a multiple linear regression model, the number of other pain disorders (P < 0.01) and a diagnosis of primary PVD (P = 0.04) were positively associated with the coital VAS pain score. Women with secondary PVD reported major improvement/complete recovery to a higher extent than women with primary PVD (z = 2.11, P = 0.04). CONCLUSION: A successful treatment outcome was more likely in PVD patients with fewer other concomitant pain conditions. The number of other bodily pain conditions was also associated to the intensity of the coital pain. Additionally, the results indicate higher incomplete response rates to treatment in women with primary PVD compared with secondary PVD.

Challenging atrophied perspectives on postmenopausal dyspareunia: a systematic description and synthesis of clinical pain characteristics.
Kao A, Binik YM, Amsel R, Funaro D, Leroux N, Khalifé S
J Sex Marital Ther. 2012 Mar;38(2):128-50.

This study investigated the clinical attributes of postmenopausal dyspareunia. The authors obtained a systematic description of pain symptomatology from 182 postmenopausal dyspareunia sufferers using a structured interview, quantitative sensory testing, a standardized pain measure, and gynecological examination. The authors conducted a cluster analysis to examine whether sufferers could be categorized using clinical pain and gynecological factors. The authors delineated 6 subgroups, each exhibiting distinct combinations of pain and gynecological characteristics. The results support the hypothesis that, similarly to premenopausal dyspareunia, postmenopausal dyspareunia is a heterogeneous condition.

Co-morbid pain conditions and feelings of invalidation and isolation among women with vulvodynia.
Nguyen RH, Ecklund AM, Maclehose RF, Veasley C, Harlow BL
Psychol Health Med. 2012 Feb 13. [Epub ahead of print]

Many women with vulvodynia also suffer from other chronic co-morbid pain conditions. Alone, these pain conditions are associated with feeling invalidated by others and feeling socially isolated. It is unclear, however, how the presence of additional pain co-morbidities are associated with the psychosocial wellbeing of women with vulvodynia. We used data from a survey administered by the National Vulvodynia Association. Women reported clinician-diagnosed vulvodynia, presence of co-morbid pain, and how often they felt that they felt no one believed their pain existed (invalidated) and isolated. Analyses determined prevalence of feeling invalidated or isolated, and the difference in prevalence when co-morbidities existed. Forty-five percent of these 1847 women with vulvodynia reported having at least one of the following five chronic pain conditions, chronic fatigue syndrome, endometriosis, fibromyalgia, interstitial cystitis, or irritable bowel syndrome. Adjusted baseline prevalence among all women of feeling invalidated was 9% and of feeling isolated was 14%. Having a co-morbid condition with vulvodynia, as well as having an increasing number of co-morbid conditions with vulvodynia, was significantly associated with the presence of feeling both invalidated and isolated. Chronic fatigue syndrome was the co-morbidity most strongly associated with feelings invalidation and isolation. One or more co-morbid pain conditions in addition to vulvodynia were significantly associated with psychosocial wellbeing. However, the temporality of the association could not be elucidated and therefore we cannot conclude that these pain conditions cause poor psychosocial wellbeing. Despite this, future studies should explore the utility of promoting validation of women's pain conditions and reducing social isolation for women with chronic pain.

Sexual behavior and oral contraception: a pilot study.
Battaglia C, Battaglia B, Mancini F, Busacchi P, Paganotto MC, Morotti E, Venturoli S
J Sex Med. 2012 Feb;9(2):550-7. doi: 10.1111/j.1743-6109.2011.02597.x.

INTRODUCTION: Oral contraceptives (OCs) induce mood and libido changes. AIM: The aim of this study was to evaluate in young, eumenorrheic, healthy women the sexual behavior and the genital vascular effects of an OC containing 30 μg ethinylestradiol (EE) and 3 mg drospirenone (DRSP). MAIN OUTCOME MEASURES: The main outcome measures are McCoy Female Sexuality Questionnaire (MFSQ), the labia minora thickness and vaginal introitus area, the pulsatility index (PI) of clitoral and labia minora arteries, and hormonal and biochemical assays. METHODS: Twenty-two adult, eumenorrheic, healthy women were administered the two-factor Italian MFSQ. The labia minora thickness was studied by two-dimensional ultrasonographic, and the clitoral and labia minora arteries were evaluated by color Doppler; three-dimensional static volumes of the vulvar area were calculated. Hormonal (estradiol, androstenedione, and testosterone) and biohumoral (sex hormone binding globulin) parameters were assayed. Subjects were studied in baseline conditions and after 3 months of therapy with an OC (Yasmin®, Bayer-Schering Italia, Milan, Italy; -30 μg EE + 3 mg DRSP). RESULTS: After 3-month treatment, the labia minora thickness and the vaginal introitus area significantly decreased in comparison with the baseline values, whereas the PI of the dorsal clitoral artery and the posterior labial artery significantly increased. The OC use induced a significant decrease of the two-factor Italian MFSQ score, a reduction of the number of intercourse/week, and a reduction of the frequency of orgasm during intercourse. The item 18 (pain during intercourse) worsened after OC. CONCLUSIONS: The treatment with Yasmin® (Bayer-Schering Italia) is associated with increased pain during intercourse, with decreased libido and spontaneous arousability, and with diminished frequency of sexual intercourse and orgasm.

Provoked vestibulodynia-women's experience of participating in a multidisciplinary vulvodynia program.
Sadownik LA, Seal BN, Brotto LA
J Sex Med. 2012 Feb 21. doi: 10.1111/j.1743-6109.2011.02641.x. [Epub ahead of print]

INTRODUCTION: Provoked Vestibulodynia (PVD) is the most common cause of pain with intercourse that affects reproductively aged women. The treatment outcome literature suggests that existing treatments, when administered

individually, may have only limited benefits for improving pain, and that multidisciplinary approaches may be more effective for reducing pain and pain-associated distress. A program that offers education, group cognitive behavioral therapy, pelvic floor physiotherapy, and medical appointments was developed and implemented at our hospital site. AIM: To explore the experiences of women who participated in the Multidisciplinary Vulvodynia Program (MVP) in order to identify the perceived benefits of this program. METHODS: Qualitative retrospective study. A semi-structured interview format was used to interview graduates of the MVP. Nineteen women, mean age 30.8 (20-54 years), participated in a one-on-one in-depth interview with a trained interviewer. The key question asked was "What has been the impact of the MVP on your life?" Interviews were audio-recorded, transcribed, and qualitatively analyzed for major themes. Main OUTCOME MEASURE: Content analysis of interview transcripts. RESULTS: Five main themes emerged and included: increased knowledge, gained tools/skills, perceived improved mood/psychological well-being, a sense of validation and support, and an enhanced sense of empowerment. CONCLUSION: Overall, a multidisciplinary vulvodynia program was perceived as being beneficial for women with PVD.

Update on the diagnosis and treatment of vulvodynia.
Itza F, Zarza D, Gómez-Sancha F, Salinas J, Bautrant E
Actas Urol Esp. 2012 Feb 23. [Epub ahead of print]

CONTEXT: Vulvodynia is a complex and multifactorial clinical condition. It is defined as chronic vulvar discomfort characterized by burning, stinging or irritation. Its diagnostic difficulty and treatment is known. OBJECTIVES: To review the medical literature of the last 10 years from a critical point of view. EVIDENCE ACQUISITION: A search was made in Medline/Pubmed and the Cochrane Library using the terms vulvodynia and vestibulodynia to which etiology, epidemiology, diagnosis, neurophysiological test and treatment or management, were added. EVIDENCE SYNTHESIS**:** In spite of the advances achieved in all of the aspects of vulvodynia, the methodology used at present in many cases does not have the desirable statistical soundness: there are few control or placebo-controlled groups and double-blind studies. Uniformity is lacking in the scales, indexes and questionnaires for the correct evaluation of pain before and after the treatment and debatable diagnostic criteria are use. The limited use of neurophysiological diagnostic resources that validate the clinical findings has been observed in the studies analyzed. In most of the works, the medical treatments have been shown to be ineffective. Physiotherapy and cognitive-behavioral therapy seem to be promising therapeutic tools. Surgery (vestibulectomy) stands out by its demonstrated efficacy in the publications studied. CONCLUSIONS: A multidisciplinary approach is always necessary. Topical medical, psychological and physical therapy treatments may have sum effects and become an alternative to surgery. New pathways of research and more regulated studies are required.

Provoked vestibulodynia: Mediators of the associations between partner responses, pain, and sexual satisfaction.
Rosen NO, Bergeron S, Lambert B, Steben M
Arch Sex Behav. 2012 Feb 16. [Epub ahead of print]

Provoked vestibulodynia (PVD) is a chronic, recurrent vulvo-vaginal pain condition affecting 12% of the general population, and is associated with sexual dysfunction, psychological distress, and reduced quality of life. There is growing interest in the role of interpersonal variables in PVD, which have been widely neglected. In a sample of 175 couples, the present study examined the mediating roles of partner and participant catastrophizing and self-efficacy in the association between solicitous partner responses and pain intensity, and that of dyadic adjustment in the association between solicitous and negative partner responses and sexual satisfaction. Couples completed measures of partner responses, catastrophizing, self-efficacy, dyadic adjustment, and depression. Women also completed measures of pain, sexual satisfaction, and sexual function. Controlling for depression and solicitousness perceived by the other member of the couple, catastrophizing and self-efficacy partially mediated the association between higher solicitous responses and higher pain during intercourse, accounting for 26 and 25% of the variance in this association for participant and partner-perceived responses, respectively. For both participant and partners, only pain catastrophizing was a unique mediator. Controlling for depression, sexual function and partner-perceived responses, dyadic adjustment partially mediated the association between higher participant-perceived solicitous responses and higher sexual

satisfaction, and between higher participant-perceived negative responses and lower sexual satisfaction, accounting for 26% of the variance in each association. The current findings suggest that catastrophizing and dyadic adjustment may constitute a route by which partner responses exacerbate pain and increase or decrease sexual satisfaction in PVD couples.

Response to pudendal nerve block in women with pudendal neuralgia.
Vancaillie T, Eggermont J, Armstrong G, Jarvis S, Liu J, Beg N
Pain Med. 2012 Mar 5. doi: 10.1111/j.1526-4637.2012.01343.x. [Epub ahead of print]

OBJECTIVE: To examine the evolution of pain and the duration of numbness after neural blockade of the pudendal nerve in women with pudendal neuralgia and correlate with clinical and historical data. DESIGN: Prospective, single arm, open label study. SETTING: University hospital and outpatient clinic. SUBJECTS: Eighty-two adult female patients were recruited from November 8, 2008 to February 14, 2010. Patients were selected based on the presence of spontaneous or provoked pain in the distribution of the pudendal nerve. INTERVENTIONS: Subjects underwent a standardized pudendal nerve block. OUTCOME MEASURES: Visual analog pain scores and the presence of numbness were recorded before and for 64 hours after the pudendal nerve block. A complete clinical history and examination were documented. RESULTS: Sixty-six patients completed the study. About 86.9% had a reduction in one or more pain symptom, while 44.3% found that more than one of their pain symptoms did not return. About 69.7% of patients reported numbness lasting up to 16 hours or longer. Previous gynecological surgery was recorded in 75.8%, previous traumatic obstetric events in 47.0% of cases. Prolonged history of pain correlated with a reduced chance of positive outcome of the pudendal nerve block. CONCLUSION: In patients with pudendal neuralgia, the pudendal nerve block has a variable response, but may have a beneficial effect in a subset of women. Surgical and obstetrical trauma are common historical antecedents.

Blockade of the ganglion impar (walther), using ultrasound and a loss of resistance technique.
Johnston PJ, Michálek P
Prague Med Rep. 2012;113(1):53-7.

The ganglion impar is an unpaired sympathetic structure located at the level of the sacrococcygeal joint. Blockade of this structure has been utilised to treat chronic perineal pain. Methods to achieve this block often involve the use of fluoroscopy which is associated with radiation exposure of staff involved in providing these procedures. We report a combined loss of resistance injection technique in association with ultrasound guidance to achieve the block. Ultrasound was used to identify the sacrococcygeal joint and a needle was shown to enter this region. Loss of resistance was then used to demonstrate that the needle tip lies in a presacral space. The implication being that any injectate would be located in an adequate position. The potential exception would be a neurodestructive procedure as radiographic control of needle tip in relation to the rectum should be performed and recorded. However when aiming for a diagnostic or local anaesthetic based treatment option we feel that this may become an accepted method.

Repeat operation for treatment of persistent pudendal nerve entrapment after pudendal neurolysis.
Hibner M, Castellanos ME, Drachman D, Balducci J
J Minim Invasive Gynecol. 2012 Feb 4. [Epub ahead of print]

STUDY OBJECTIVES: To describe a new approach to transgluteal pudendal neurolysis and transposition and to review the outcome in 10 patients who underwent repeat operation because of persistent pudendal neuralgia after failing to improve after initial surgical decompression. DESIGN: Retrospective analysis (Canadian Task Force classification II-3). SETTING: Academic chronic pelvic pain practice at St. Joseph's Hospital and Medical Center in Phoenix, Arizona. PATIENTS: Women and men with persistent pudendal neuralgia after undergoing transgluteal pudendal neurolysis and transposition. INTERVENTION: Transgluteal decompression of the pudendal nerve was performed in all 10 patients. In

brief, a transgluteal incision was made, and the pudendal nerve was identified via a nerve integrity monitoring system. Adhesiolysis was performed from the piriformis muscle to the distal Alcock canal using a Zeiss NC-4 surgical microscope. The nerve was then enclosed in NeuraWrap Nerve Protector and coated with activated platelet-rich plasma. An ON-Q PainBuster catheter was place along the nerve into the Alcock canal, and 0.5% bupivacaine was infused at 2 mL/hr. The sacrotuberous ligament was repaired using an Achilles or gracillis cadaver ligament. The overlying subcutaneous tissue and skin were then closed. MEASUREMENTS AND MAIN RESULTS**:** From June 2008 to March 2010, 10 consecutive patients (7 women and 3 men; age range, 29-81 years) underwent repeat operation with transgluteal decompression of the pudendal nerve. Neuropathic pain was unilateral (n = 8) or bilateral (n = 2), in the clitoris or penis (30%), vulva or scrotum (70%), perineum (40%), and rectum (50%). Of the 10 patients, 1 patient was lost to follow-up. Mean follow-up was 23 months. Eight of 9 patients reported global improvement, with 2 patients reporting complete resolution of symptoms. One patient reported no change. Pain, as measured using an 11-point numerical scale, improved from a mean of 7.2 to 4.0 (p = .02), with 5 patients reporting clinically significant improvement (change, ≥2). Comfortable sitting or maximum time that the patient was able to sit without exacerbation of pain improved in 8 patients, with a change in median time of 5 to 45 minutes (p = .008). Change in the ability to sit correlated well with patient-reported global improvement (correlation coefficient, 0.86). No patient experienced worsening of symptoms. CONCLUSION: Patients with persistent pudendal neuralgia after surgical decompression may benefit from repeat operation via our novel approach. Ability to sit correlates well with reported improvement due to surgery.

Randomized controlled trial comparing pudendal nerve block under ultrasound and fluoroscopic guidance.
Bellingham GA, Bhatia A, Chan CW, Peng PW
Reg Anesth Pain Med. 2012 Mar 16.

BACKGROUND: Although fluoroscopy is an established imaging modality for pudendal nerve block, ultrasound (US) technique allows physicians better visualization of anatomic structures. This study aimed to compare the effectiveness and safety between the US- and fluoroscopy-guided techniques. METHODS: A randomized, single-blind, split-plot design was used to conduct the study. Twenty-three patients undergoing bilateral pudendal nerve blocks received US-guided injections to either the left or right side, whereas the contralateral side received a fluoroscopic-guided injection in randomized sequence. Injections consisted of 4 mL of 0.5% bupivacaine and 40 mg methylprednisone. The primary outcome was the success of the block in the distribution of the pudendal nerve along the perineum, rated as either absent, moderate, or strong. Secondary outcomes were the time to administer the blocks, quality of visualization of anatomic structures using US and fluoroscopy, distance of the final US-guided needle position from the ischial spine, and incidence of adverse effects. RESULTS: No differences in the degree of neural blockade were noted between US- or fluoroscopic-guided techniques for either temperature or pinprick blockade. Time to complete the procedure was significantly longer using US compared with fluoroscopy (219 [SD, 65] and 428 [SD, 151] secs, P < 0.0001). No significant differences were noted regarding the occurrence of adverse effects between the 2 techniques. CONCLUSIONS: Ultrasound-guided pudendal nerve blockade is as accurate as fluoroscopically guided injections when performed by an experienced clinician. However, the former took a longer time to perform.

Genitofemoral and perineal neuralgia after transobturator midurethral sling.
Parnell BA, Johnson EA, Zolnoun DA
Obstet Gynecol. 2012 Feb;119(2 Pt 2):428-31.

BACKGROUND: Midurethral slings successfully treat stress urinary incontinence through a minimally invasive vaginal approach. Postoperative pain related to sling placement can occur and poses both diagnostic and treatment dilemmas. CASE: Four years after transobturator midurethral sling placement, the patient presented with complaints of left labial pain and dyspareunia since surgery. Using sensory mapping and a nerve stimulator, the problem was identified in the distribution of the genitofemoral nerve. Conservative therapy with a centrally acting neuromodulatory drug and nerve block relieved the pain. CONCLUSION: Postsling neuralgia diagnosis using sensory mapping and a nerve stimulator aids in indentifying the nerve involved and in successful conservative treatment with a nerve block.

Peripheral nerve toxic effects of nitrofurantoin.
Tan IL, Polydefkis MJ, Ebenezer GJ, Hauer P, McArthur JC
Arch Neurol. 2012 Feb;69(2):265-8.

OBJECTIVE: To investigate the role of skin biopsy in nitrofurantoin peripheral neuropathy. DESIGN: We describe the clinical features and skin biopsies of 2 cases of non-length-dependent small-fiber neuropathy/ganglionopathy attributable to nitrofurantoin. SETTING: Clinical evaluation and skin biopsies were performed at a tertiary teaching hospital in Baltimore, Maryland. Patients A 59-year-old woman with disabling generalized dysesthesia and a 53-year-old woman with progressive burning pain in the perineum and extremities. MAIN OUTCOME MEASURES: Slow or incomplete recovery and possibly irreversible damage. RESULTS: The neuropathy was neither dose dependent nor associated with impaired renal function. Results from nerve conduction studies were normal. Skin biopsies revealed distinctive morphologic changes with clustered terminal nerve swellings without evidence of nerve fiber degeneration. CONCLUSIONS: These distinct morphologic changes associated with nitrofurantoin have not been previously reported to our knowledge. Skin biopsy appears to be helpful in confirming the diagnosis in these patients.

A qualitative study of heterosexual women's attempts to renegotiate sexual relationships in the context of severe sexual problems.
Hinchliff S, Gott M, Wylie K
Arch Sex Behav. 2012 Feb 9. [Epub ahead of print]

Previous qualitative research on women's sexual problems has documented the ways in which they can impact psychological well-being as well as women's close interpersonal relationships. However, little attention has been paid to the ways that women with sexual problems negotiate sexual contact in the context of a relationship where sexual activity has a central role. This article draws on qualitative data from in-depth interviews with 23 heterosexual women who experienced sexual desire loss or vulvar pain. The data were analyzed within a material-discursive framework and this identified the centrality of relational and broader social factors in women's sexual negotiation. Key findings included: avoiding potentially intimate situations; engaging in intercourse when it was painful or the women had no desire to; and mentally planning and preparing themselves for sex. Other sexual activities were almost always regarded as a prelude to intercourse, yet around half of the sample had adapted their sexual repertoire to compensate for an absence of intercourse. The implications for future research and treatment in the area of women's sexual problems are discussed.

Sexual function and distress in women treated for primary headaches in a tertiary university center.
Nappi RE, Terreno E, Tassorelli C, Sances G, Allena M, Guaschino E, Antonaci F, Albani F, Polatti F
J Sex Med. 2012 Mar;9(3):761-769. doi: 10.1111/j.1743-6109.2011.02601.x.

INTRODUCTION: Primary headaches are common in women and impact on their quality of life and psychosocial functioning. Few data are available on sexuality in female headache sufferers. AIM: An observational pilot study was conducted to assess sexual function and distress in women treated for primary headaches in a tertiary university center. METHODS: From a total of 194 women consecutively observed over a 3-month period, 100 patients were recruited. Migraine with and without aura, and tension-type headache, both episodic and chronic (CTTH), were diagnosed according to the International Classification of Headache Disorders. A detailed pharmacological history was collected, and anxiety and depression were assessed using validated scales. The Female Sexual Function Index (FSFI) and Female Sexual Distress Scale-Revised were administered. MAIN OUTCOME MEASURES: The main outcome measures are sexual symptoms and distress in women treated for primary headaches. RESULTS: More than 90% of the women had a median FSFI full-scale score under the validated cutoff, while 29% reported sexual distress. Hypoactive sexual desire disorder (HSDD) was diagnosed in 20% of the women and the pain domain score (median 2, score range 0-6) was highly affected by the head pain condition. However, the FSFI domain and full-scale scores did not significantly differ by headache diagnosis. The women with CTTH displayed a high rate of sexual distress (45.5%) and a strong negative correlation

between desire, arousal, and full-scale FSFI score and number analgesics/month (r: -0.77, P = 0.006; r: -0.76, P = 0.006; and r: -0.68, P = 0.02, respectively). Depression was positively correlated with sexual distress (r: 0.63, P = 0.001) only in the women with CTTH. CONCLUSION: Women treated for primary headaches were found to display a high rate of sexual symptoms and distress. Both migraine and tension-type headache were associated with sexual pain and HSDD, but women with CTTH seem to be more prone to develop sexual distress.

Recognition and management of nonrelaxing pelvic floor dysfunction.
Faubion SS, Shuster LT, Bharucha AE
Mayo Clin Proc. 2012 Feb;87(2):187-93.

Nonrelaxing pelvic floor dysfunction is not widely recognized. Unlike in pelvic floor disorders caused by relaxed muscles (eg, pelvic organ prolapse or urinary incontinence, both of which often are identified readily), women affected by nonrelaxing pelvic floor dysfunction may present with a broad range of nonspecific symptoms. These may include pain and problems with defecation, urination, and sexual function, which require relaxation and coordination of pelvic floor muscles and urinary and anal sphincters. These symptoms may adversely affect quality of life. Focus on the global symptom complex, rather than the individual symptoms, may help the clinician identify the condition. The primary care provider is in a position to intervene early, efficiently, and effectively by (1) recognizing the range of symptoms that might suggest nonrelaxing pelvic floor dysfunction, (2) educating patients, (3) performing selective tests when needed to confirm the diagnosis, and (4) providing early referral for physical therapy.

Evaluation of sexual function in Brazilian women with recurrent vulvovaginal candidiasis and localized provoked vulvodynia.
Giraldo PC, Polpeta NC, Juliato CR, Yoshida LP, Amaral RL, Junior JE
J Sex Med. 2012 Mar;9(3):805-11. doi: 10.1111/j.1743-6109.2011.02584.x.

INTRODUCTION: Recurrent vulvovaginitis is an important trigger for inflammatory processes that in many cases may result in vulvovaginal pain. Vulvodynia, a vulvar disorder, can also cause a lot of pain in the female genitals. The sexual function in women with vulvodynia or recurrent vulvovaginitis will possibly be negatively affected and therefore should be evaluated. AIM: To assess sexual function in women with recurrent vulvovaginal candidiasis (RVVC) and localized provoked vulvodynia (LPV) in comparison with women without lower genital tract dysfunction. METHODS: A 1-year cross-sectional study evaluated sexual function in 58 women (11 with RVVC, 18 with LPV, and 29 controls) seen at a university outpatient clinic. Sexual function was assessed by taking into account the results obtained from the application of the Female Sexual Function Index (FSFI) questionnaire. Kruskal-Wallis, Mann-Whitney, chi-square, and Fisher's tests were used for statistical analysis. MAIN OUTCOME MEASURE: FSFI, a validated questionnaire in Portuguese. RESULTS: There were no significant differences in the three groups with respect to age, marital status, schooling, race, body mass index, contraceptive method, and parity. The FSFI questionnaire total score found was 25.51 (±5.12), 21.17 (±5.15), and 29.56 (±3.87) for the RVVC, LPV, and control groups, respectively. The scores were significantly statistically lower in the study groups compared with the control group (P < 0.05). Women with RVVC and LPV also had lower total scores compared with 26.55 values, considered a cutoff score for sexual dysfunction in literature. The LPV group showed a significant difference and scored worse in the domains of arousal, lubrication, orgasm, satisfaction, and pain but not in the domain of sexual desire. The same occurred with the RVVC group but only for the domains of orgasm and satisfaction. CONCLUSION: Women with RVVC and LPV had significantly more symptoms of sexual dysfunction than women without lower genital tract diseases.

Multivariate analysis of dyspareunia in women [Article in Chinese].
Zhang AX, Chen XY, Pan LJ, Lei Y, Kan YJ
Zhonghua Nan Ke Xue. 2011 Dec;17(12):1073-7.

OBJECTIVE: Dyspareunia is a common sexual trouble in women during the sexual intercourse. This study is to investigate the risk factors for dyspareunia in urban Chinese women and to supply some evidence for its preventive measures. METHODS: We conducted a hospital-based survey by distributing 2 658 copies of a questionnaire among the women in Nanjing urban area who came for regular physical examination in Nanjing Maternity and Child Health Hospital and their female companions aged over 20 years. The sexual function of the subjects was evaluated according to female sexual function indexes, dyspareunia indicated by sexual pain score < 4.4, and the results analyzed by multiple logistic regression analysis. RESULTS: Totally, 1 856 (69.8%) of the subjects completed the questionnaire, and 1 457 that met the criteria were included for analysis, of whom 43.0% (626/1457) admitted to dyspareunia during the sexual intercourse. Multiple logistic regression analysis showed that age (> or = 50 years), smoking, hysterectomy, vaginal lubrication disorder, lack of sexual communication with partners were independent risk factors for dyspareunia (P < 0.05). CONCLUSION: Dyspareunia is associated with multiple factors including age (> or = 50 years), smoking, hysterectomy, vaginal lubrication disorder, lack of sexual communication with partners.

Basic Science/Anatomy

Systemic and topical hormone therapies reduce vaginal innervation density in postmenopausal women.
Griebling TL, Liao Z, Smith PG
Menopause. 2011 Dec 27. [Epub ahead of print]

OBJECTIVE: Menopause is often accompanied by vaginal discomfort including burning, itching, dryness, and spontaneous or provoked pain. Although the direct effects of estrogen withdrawal on vaginal cells are implicated, surgical menopause in rodents causes autonomic and sensory nerves to proliferate, suggesting that indirect effects mediated by changes in vaginal innervation may contribute. We assessed whether postmenopausal women display hormone-dependent changes in vaginal innervation. METHODS: Vaginal biopsies from 20 postmenopausal women undergoing surgery for stress urinary incontinence and pelvic organ prolapse were fixed and immunostained for the pan-neuronal marker protein gene product 9.5, sympathetic marker tyrosine hydroxylase, parasympathetic marker vasoactive intestinal polypeptide, and sensory nociceptor marker calcitonin gene-related peptide. Innervation density was measured as an apparent percentage of the section area occupied by immunofluorescent axons. Specimens were grouped according to whether participants received systemic hormone therapy (HT), topical (vaginal) HT, or no HT. RESULTS: Women not receiving HT showed relatively high levels of total innervation, with most axons expressing tyrosine hydroxylase or vasoactive intestinal polypeptide immunoreactivity. In women receiving systemic HT, overall innervation was reduced, as were presumptive parasympathetic, sympathetic, and sensory axon populations. Topical HT elicited more dramatic reductions in innervation than in systemic HT. CONCLUSIONS: Hormone therapy reduces autonomic and sensory vaginal innervation density, which may, in part, contribute to relief from vaginal discomfort. Moreover, topical therapy is more effective than systemic therapy, which may help explain the greater improvement reported with topical compared with systemic HT.

Pain

Pain mechanisms in patients with chronic pain.
Fornasari D
Clin Drug Investig. 2012 Feb 22;32 Suppl 1:45-52. doi: 10.2165/11630070-000000000-00000.

The mechanisms involved in the development of chronic pain are varied and complex. Pain processes are plastic and unrelieved pain may lead to changes in the neural structure involved in pain generation. Nociceptive pain announces the presence of a potentially damaging stimulus that occurs when noxious stimuli activate primary afferent neurons. Neuropathic pain is initiated or caused by a primary lesion or dysfunction in the nervous system resulting from trauma, infection, ischaemia, cancer or other causes such as chemotherapy. The exact mechanisms involved in the pathophysiology of chronic pain are not well understood, but rapid and long-term changes are thought to occur in parts of the central nervous system that are involved in the transmission and modulation of pain following injury. Peripheral and central sensitization of sensory nerve fibres are the primary reasons for hypersensitivity to pain after injury, and mainly occur in inflammatory and neuropathic pain. During these processes the sensation of pain is enhanced as a result of changes in the environment, the nerve fibres and modifications of the functional properties and the genetic programme of primary and secondary afferent neurons. Non-steroidal anti-inflammatory drugs and opioid analgesics are two of the most common classes of drugs used for the treatment of pain. Response to drug treatment shows significant interindividual variability and can lead to side effects. The neurobiological mechanisms that cause pain may account for the different types of pain observed. Identification of these mechanisms may allow us to move from an empirical therapeutic approach to one that it is specifically targeted at the particular mechanisms of the type of pain experienced by an individual patient.

Central nervous system reorganization in a variety of chronic pain states: a review.
Henry DE, Chiodo AE, Yang W
PM R. 2011 Dec;3(12):1116-25.

Chronic pain can develop from numerous conditions and is one of the most widespread and disabling health problems today. Unfortunately, the pathophysiology of chronic pain in most of these conditions, along with consistently effective treatments, remain elusive. However, recent advances in neuroimaging and neurophysiology are rapidly expanding our understanding of these pain syndromes. It is now clear that substantial functional and structural changes, or plasticity, in the central nervous system (CNS) are associated with many chronic pain syndromes. A group of cortical and subcortical brain regions, often referred to as the "pain matrix," often show abnormalities on functional imaging studies in persons with chronic pain, even with different pain locations and etiologies. Changes in the motor and sensory homunculus also are seen. Some of these CNS changes return to a normal state with resolution of the pain. It is hoped that this knowledge will lead to more effective treatments or even new preventative measures. The purpose of this article is to review recent advances in the understanding of the CNS changes associated with chronic pain in a number of clinical entities encountered in the field of physical medicine and rehabilitation. These clinical entities include nonspecific low back pain, fibromyalgia, complex regional pain syndrome, postamputation phantom pain, and chronic pain after spinal cord injury.

The role of sodium channels in chronic pain.
Levinson S, Luo S, Henry M
Musc & Nerve. 2012 Jan 24.

Here we review recent research into the mechanisms of chronic pain that has focused on neuronal sodium channels, a target of classic analgesic agents. We first discuss evidence that specific sodium channel isoforms are essential for the detection and conduction of normal acutely painful stimuli from nociceptors. We then review findings that show changes in sodium channel expression and localization in chronic inflammation and nerve injury in animal and human

tissues. We conclude by discussing the role that myelination plays in organizing and maintaining sodium channel clusters at nodes of Ranvier in normal development and how inflammatory processes or nerve injury alter the characteristics of such clusters. Based on these findings, we suggest that chronic pain may in part result from partial demyelination of axons during chronic injury, which creates aberrant sodium channel clusters that serve as sites of ectopic sensitivity or spontaneous activity.

HCN2 ion channel plays a central role in inflammatory and neuropathic pain.
Emery EC, Young GT, Berrocoso EM, Chen L, McNaughton PA
Science. 2011 Sep 9;333(6048):1462-6.

The rate of action potential firing in nociceptors is a major determinant of the intensity of pain. Possible modulators of action potential firing include the HCN ion channels, which generate an inward current, Ih, after hyperpolarization of the membrane. We found that genetic deletion of HCN2 removed the cyclic adenosine monophosphate (cAMP)–sensitive component of Ih and abolished action potential firing caused by an elevation of cAMP in nociceptors. Mice in which HCN2 was specifically deleted in nociceptors expressing NaV1.8 had normal pain thresholds, but inflammation did not cause hyperalgesia to heat stimuli. After a nerve lesion, these mice showed no neuropathic pain in response to thermal or mechanical stimuli. Neuropathic pain is therefore initiated by HCN2-driven action potential firing in NaV1.8-expressing nociceptors.

Estrogen and visceral nociception at the level of primary sensory neurons.
Chaban V
Pain Res Treat. 2012 Jan 1;2012(2012). pii: 960780.

Clinical studies suggest the comorbidity of functional pain syndromes such as irritable bowel syndrome, painful bladder syndrome, chronic pelvic pain, and somatoform disorders approaches 40% to 60%. The incidence of episodic or persistent visceral pain associated with these "functional" disorders is two to three times higher in women than in men. One of the possible explanations for this phenomenon is estrogen modulation of viscerovisceral cross-sensitization. While a central site of this modulation has been shown previously, our studies suggest a peripheral site, the dorsal root ganglion (DRG). Estrogens have remarkably wide range of functions including modulation of voltage-gated calcium channels (VGCCs) and purinoreceptors (P2Xs). Significantly, inflammation dramatically alters purinoception by causing a several fold increase in ATP-activated current, alters the voltage dependence of P2X receptors, and enhances the expression of P2X receptors increasing neuronal hypersensitivity. Gonadal hormones are thought as indispensable cornerstones of the normal development and function, but it appears that no body region, no neuronal circuit, and virtually no cell is unaffected by them. Thus, increasing awareness toward estrogens appears to be obligatory.

Sex differences in reported pain across 11,000 patients captured in electronic medical records.
Ruau D, Liu LY, Clark JD, Angst MS, Butte AJ
J Pain. 2012 Jan 13. [Epub ahead of print]

Clinically recorded pain scores are abundant in patient health records but are rarely used in research. The use of this information could help improve clinical outcomes. For example, a recent report by the Institute of Medicine stated that ineffective use of clinical information contributes to undertreatment of patient subpopulations-especially women. This study used diagnosis-associated pain scores from a large hospital database to document sex differences in reported pain. We used de-identified electronic medical records from Stanford Hospital and Clinics for more than 72,000 patients. Each record contained at least 1 disease-associated pain score. We found over 160,000 pain scores in more than 250 primary diagnoses, and analyzed differences in disease-specific pain reported by men and women. After filtering for diagnoses with minimum encounter numbers, we found diagnosis-specific sex differences in reported pain. The most significant differences occurred in patients with disorders of the musculoskeletal, circulatory, respiratory and digestive

systems, followed by infectious diseases, and injury and poisoning. We also discovered sex-specific differences in pain intensity in previously unreported diseases, including disorders of the cervical region, and acute sinusitis (P = .01, .017, respectively). Pain scores were collected during hospital encounters. No information about the use of pre-encounter over-the-counter medications was available. To our knowledge, this is the largest data-driven study documenting sex differences of disease-associated pain. It highlights the utility of electronic medical record data to corroborate and expand on results of smaller clinical studies. Our findings emphasize the need for future research examining the mechanisms underlying differences in pain. PERSPECTIVE: This article highlights the potential of electronic medical records to conduct large-scale pain studies. Our results are consistent with previous studies reporting pain differences between sexes and also suggest that clinicians should pay increased attention to this idea.

The effects of sex and gender role on responses to pressure pain.
Kröner-Herwig B, Gaßmann J, Tromsdorf M, Zahrend E
Psychosoc Med. 2012;9:Doc01. Epub 2012 Feb 28.

BACKGROUND: Several studies on experimental mechanical pain suggested a strong influence of sex demonstrating females to be more sensitive. We examined the hypothesis that not only sex but also gender role affects pain responsiveness and looked for mediators of this effect. METHOD: As indicators of pain the threshold the intensity and the unpleasantness of pressure stimuli were measured, as well as sensory and affective quality of pain. The gender role of 74 students was assessed by the Bem Sex Role Inventory (BSRI). Furthermore several psychological variables assumed to be potential mediators (catastrophising, fear of pain, depressive symptoms, pain coping) were obtained. RESULTS: ANOVA revealed significant main effects of sex in all pain variables except affective quality of pain. Contrary to our hypothesis gender role had no influence on pain responses, neither was there an interaction of sex and gender. Fear of pain just missed the significance level identifying it as mediator of the sex effect on affective pain. CONCLUSIONS: In summary, our study corroborated previous findings that women are more responsive to mechanical pain stimuli with effect sizes being medium to large, whereas gender role did not predict any of the assessed pain parameters. No convincing evidence was found that the influence of sex is predominantly mediated by psychological characteristics of the individual.

Menopause affects pain depending on pain type and characteristics.
Meriggiola MC, Nanni M, Bachiocco V, Vodo S, Aloisi AM
Menopause. 2012 Feb 13. [Epub ahead of print]

OBJECTIVE: Women are more affected than men by many chronic pain conditions, suggesting the effect of sex-related mechanisms in their occurrence. The role of gonadal hormones has been studied but with contrasting results depending on the pain syndrome, reproductive status, and hormone considered. The aim of the present study was to evaluate the pain changes related to the menopausal transition period. METHODS: In this observational study, postmenopausal women were asked to evaluate the presence of pain in their life during the premenopausal and postmenopausal periods and its modification with menopause. RESULTS: One hundred one women were enrolled and completed questionnaires on their sociodemographic status, pain characteristics, and evolution. The most common pain syndromes were headache (38%), osteoarticular pain (31%), and cervical/lumbar pain (21%). Pain was present before menopause in 66 women, ceased with menopause in 17, and started after menopause in 18. Data were used for cluster analysis, which allowed the division of participants into four groups. In the first, all women experienced headaches that disappeared or improved with menopause. The second group included osteoarticular pain; the pain improved in half of these women and remained stable in the other half. The third group had cervical/lumbar pain, which disappeared or improved with menopause in all. The fourth group presented different kinds of moderate pain, which worsened in all. CONCLUSIONS: The present study provides preliminary data suggesting that menopause can affect pain depending on the painful condition experienced by the woman. This underlines the different interactions of menopause-related events with body structures involved in pain.

Behavioural and neural correlates of visceral pain sensitivity in healthy men and women: Does sex matter?
Benson S, Kotsis V, Rosenberger C, Bingel U, Forsting M, Schedlowski M, Gizewski ER, Elsenbruch S
Eur J Pain. 2011 Dec 19. doi: 10.1002/j.1532-2149.2011.00027.x. [Epub ahead of print]

INTRODUCTION: We assessed sex differences in behavioural and neural responses to rectal pain stimuli in healthy subjects. METHODS: In age- and body mass index-matched healthy subjects (n = 15 men, 15 women), rectal sensory and pain thresholds were assessed with a pressure-controlled barostat device. The blood oxygen level-dependent response during cued anticipation and painful stimulation was measured using functional magnetic resonance imaging (fMRI). Retrospective pain evaluations were accomplished with visual analogue scales. For fMRI data, region-of-interest (ROI) analyses and additional whole-brain analyses were carried out. RESULTS: There were no sex differences in rectal thresholds or pain ratings. ROI analyses revealed comparable distension-induced activation of the thalamus, somatosensory cortex, insula and dorsolateral prefrontal cortex (DLPFC). Only in additional whole-brain analyses did we find increased activation in women in DLPFC and middle temporal gyrus during pain anticipation and in the cerebellum and medial frontal gyrus during pain. A significant inverse association between rectal pain threshold and distension-induced activation in virtually all ROIs was found in women. In men, pain thresholds and insula activation were positively correlated, as were pain ratings and anterior cingulate cortex activation. CONCLUSIONS: Healthy men and women do not differ in behavioural measures of visceral pain sensitivity. The pattern of neural activation is comparable in the majority of pain-processing brain regions, although women may differ in the activation of DLPFC which could reflect sex differences in cognitive-emotional pain regulation. Women with lower pain thresholds showed greater neural responses, which may be relevant in the pathophysiology of visceral hyperalgesia.

A systematic literature review of 10 years of research on sex/gender and experimental pain perception - Part 1: Are there really differences between women and men?
Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M
Pain. 2012 Mar;153(3):602-18.

The purpose of this systematic review was to summarize and critically appraise the results of 10 years of human laboratory research on pain and sex/gender. An electronic search strategy was designed by a medical librarian and conducted in multiple databases. A total of 172 articles published between 1998 and 2008 were retrieved, analyzed, and synthesized. The first set of results (122 articles), which is presented in this paper, examined sex difference in the perception of laboratory-induced thermal, pressure, ischemic, muscle, electrical, chemical, and visceral pain in healthy subjects. This review suggests that females (F) and males (M) have comparable thresholds for cold and ischemic pain, while pressure pain thresholds are lower in F than M. There is strong evidence that F tolerate less thermal (heat, cold) and pressure pain than M but it is not the case for tolerance to ischemic pain, which is comparable in both sexes. The majority of the studies that measured pain intensity and unpleasantness showed no sex difference in many pain modalities. In summary, 10years of laboratory research have not been successful in producing a clear and consistent pattern of sex differences in human pain sensitivity, even with the use of deep, tonic, long-lasting stimuli, which are known to better mimic clinical pain. Whether laboratory studies in healthy subjects are the best paradigm to investigate sex differences in pain perception is open to question and should be discussed with a view to enhancing the clinical relevance of these experiments and developing new research avenues.

A systematic literature review of 10 years of research on sex/gender and pain perception - Part 2: Do biopsychosocial factors alter pain sensitivity differently in women and men?
Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M
Pain. 2012 Mar;153(3):619-35.

This systematic review summarizes the results of 10 years of laboratory research on pain and sex/gender. An electronic search strategy was designed by a medical librarian to access multiple databases. A total of 172 articles published between 1998 and 2008 were retrieved, analyzed, and synthesized. The second set of results presented in this review

(129 articles) examined various biopsychosocial factors that may contribute to differences in pain sensitivity between healthy women and men. The results revealed that the involvement of hormonal and physiological factors is either inconsistent or absent. Some studies suggest that temporal summation, allodynia, and secondary hyperalgesia may be more pronounced in women than in men. The evidence to support less efficient endogenous pain inhibitory systems in women is mixed and does not necessarily apply to all pain modalities. With regard to psychological factors, depression may not mediate sex differences in pain perception, while the role of anxiety is ambiguous. Cognitive and social factors appear to partly explain some sex-related differences. Finally, past individual history may be influential in female pain responses. However, these conclusions must be treated with much circumspection for various methodological reasons. Furthermore, some factors/mechanisms remain understudied in the field. There is also a need to assess and improve the ecological validity of findings from laboratory studies on healthy subjects, and perhaps a change of paradigm needs to be considered at this point in time to better understand the factors that influence the experience of women and men who suffer from acute or chronic pain.

The perception of pain in others: How gender, race, and age influence pain expectations.
Wandner LD, Scipio CD, Hirsh AT, Torres CA, Robinson ME
J Pain. 2012 Jan 5. [Epub ahead of print]

Sex, race/ethnic, and age differences in pain have been reported in clinical and experimental research. Gender role expectations have partly explained the variability in sex differences in pain, and the Gender Role Expectations of Pain questionnaire (GREP) was developed to measure sex-related stereotypic attributions about pain. It is hypothesized that similar expectations exist for age- and race-related pain decisions. This study investigated new measures of race/ethnic- and age-related stereotypic attributions of pain sensitivity and willingness to report pain, and examined the psychometric properties of a modified GREP. Participants completed the Race/Ethnicity Expectations of Pain questionnaire, Age Expectations of Pain questionnaire, and modified GREP. Results revealed a 3-factor solution to the race/ethnicity questionnaire and a 2-factor solution to the age questionnaire, consistent with theoretical construction of the items. Results revealed a 4-factor solution to the modified GREP that differed from the original GREP and theoretical construction of the items. Participants' pain-related stereotypic attributions differed across racial/ethnic, age, and gender groups. These findings provide psychometric support for the measures examined herein and suggest that stereotypic attributions of pain in others differ across demographic categories. Future work can refine the measures and examine whether select demographic variables influence pain perception, assessment, and/or treatment. PERSPECTIVE: The findings suggest that one's expectations of the pain experience of another person are influenced by the stereotypes one has about different genders, races, and ages. The 3 pain expectation measures investigated in the current study could be used in future work examining biases in pain assessment and treatment.

Persistent pain: not a medically unexplained symptom.
Williams AC, Johnson M
Br J Gen Pract. 2011 Oct;61(591):638-9.

No abstract available.

The prevalence of fibromyalgia in other chronic pain conditions.
Yunus MB
Pain Res Treat. 2012;2012:584573.

Central sensitivity syndromes (CSS) include fibromyalgia syndrome (FMS), irritable bowel syndrome, temporomandibular disorder, restless legs syndrome, chronic fatigue syndrome, and other similar chronic painful conditions that are based on central sensitization (CS). CSS are mutually associated. In this paper, prevalence of FMS among other members of CSS has been described. An important recent recognition is an increased prevalence of FMS in other chronic pain conditions

with structural pathology, for example, rheumatoid arthritis, systemic lupus, ankylosing spondylitis, osteoarthritis, diabetes mellitus, and inflammatory bowel disease. Diagnosis and proper management of FMS among these diseases are of crucial importance so that unwarranted use of such medications as corticosteroids can be avoided, since FMS often occurs when RA or SLE is relatively mild.

Neuropathic pain: An evolutionary hypothesis.
Ashton JC
Med Hypotheses. 2012 Feb 17. [Epub ahead of print]

BACKGROUND: Whereas nociceptive pain has a clear survival value, the evolutionary origins of neuropathic pain remains unexplained. OBJECTIVES**:** It is argued that neuropathic pain is an adaptation that has evolved to detect non-specific damage to the nervous system, and that it operates on the same principles of an analogous hypothesis that has been put forward to explain the evolutionary utility of motion sickness. Whereas motion sickness has been proposed to arise from an inappropriate activation of a system evolved to respond to incoherence between vestibular and visual reference frames as an indication of acute neurotoxicity, it is proposed that neuropathic pain arises from the activation of a system evolved to respond to incoherence between proprioceptive and motor outputs as an indication of nerve trauma. RESULTS AND CONCLUSIONS: Evidence that supports this hypothesis is reviewed, followed by conclusions regarding consequences for pain theory and management.

Pharmacology update: Tapentadol for neuropathic pain.
Pierce DM, Shipstone E
Am J Hosp Palliat Care. 2012 Feb 23. [Epub ahead of print]

Neuropathic pain in a common problem encountered in palliative care. When neuropathic pain is diagnosed, appropriate treatment is important in limiting the severe psychosocial impairment that can ensue with undertreated pain. Proper evaluation of the patient to clarify the type of pain experienced is the first step to determine appropriate management. Tapentadol is an oral mu-opioid receptor agonist and a noradrenaline reuptake inhibitor developed by Ortho-McNeil Janssen Pharmaceuticals and approved by the Food and Drug Administration in November 2008 for the treatment of moderate-to-severe acute pain in adult patients and for chronic pain in August 2011 in an extended release form. Tapentadol has been studied for use in nociceptive pain but few studies have yet been done to assess its efficacy in the treatment of neuropathic pain.

Cannabinoids and muscular pain. Effectiveness of the local administration in rat.
Sánchez Robles EM, Bagües Arias A, Martín Fontelles MI
Eur J Pain. 2012 Feb 21. doi: 10.1002/j.1532-2149.2012.00115.x. [Epub ahead of print]

BACKGROUND: Pain associated with musculoskeletal disorders can be difficult to control and the incorporation of new approaches for its treatment is an interesting challenge. Activation of cannabinoid (CB) receptors decreases nociceptive transmission in acute, inflammatory and neuropathic pain states; however, although the use of cannabis derivatives has been recently accepted as a useful alternative for the treatment of spasticity and pain in patients with multiple sclerosis, the effects of CB receptor agonists in muscular pain have hardly been studied. METHODS: Here, we characterized the antinociceptive effect of non selective and selective CB agonists by systemic and local administration, in two muscular models of pain, masseter and gastrocnemius, induced by hypertonic saline (HS) injection. Drugs used were: the non-selective agonist WIN 55,212-2 and two selective agonists, ACEA (CB (1)) and JWH 015 (CB (2)); AM 251 (CB (1)) and AM 630 (CB (2)) were used as selective antagonists. RESULTS: In the masseter pain model, both systemic (intraperitoneal) and local (intramuscular) administration of CB (1) and CB (2) agonists reduced the nociceptive behaviour induced by HS, whereas in the gastrocnemius model the local administration was more effective than systemic. CONCLUSIONS: Our results provide evidence that both, CB (1) and CB (2) receptors can contribute to muscular

antinociception and, interestingly, suggest that the local administration of CB agonists could be a new and useful pharmacological strategy in the treatment of muscular pain, avoiding adverse effects induced by systemic administration.

Prevalence of fibromyalgia syndrome in patients referred to a tertiary pain clinic.
Brill S, Ablin JN, Goor-Aryeh I, Hyat K, Slefer A, Buskila D
J Investig Med. 2012 Feb 27. [Epub ahead of print]

BACKGROUND: Fibromyalgia syndrome (FMS), the prototypical central pain augmentation syndrome, is characterized by widespread pain and tenderness. Although patients referred to tertiary care pain clinics are recognized as suffering from chronic pain, they are generally considered to have pain attributable to discrete peripheral, nociceptive, or neuropathic etiology. The purpose of the current study was to assess the prevalence of FMS among consecutive patients referred to a tertiary pain clinic and to evaluate the contribution of central pain to the clinical impact upon such patients. METHODS: Eighty-five consecutive patients (38 were male, and 47 were female) attending a pain clinic were assessed for the presence of FMS. The presence of FMS was determined according to the 1990 American College of Rheumatology (ACR) classification criteria. Quality of life and physical functioning were assessed, utilizing a structured questionnaire. RESULTS: The ACR criteria for the classification of FMS were fulfilled by 41.2% of patients. Patients fulfilling FMS criteria ranked significantly lower on all domains of the SF-36, including general health, physical functioning, role limitation due to physical and emotional problems, vitality, social functioning, bodily pain, and mental health. Composite physical and mental health scores were significantly lower among patients fulfilling ACR FMS criteria. Patients fulfilling the ACR criteria for FMS felt significantly more tenderness, based on the mean number of tender points and the mean tenderness threshold, when compared with patients not fulfilling the ACR FMS criteria. CONCLUSIONS: A significant proportion of patients referred to a tertiary pain clinic were found to fulfill the ACR criteria for classification of FMS and thus exhibit an important element of central pain. *Central pain augmentation should be actively searched for and therapeutically addressed in the evaluation and management of all patients with chronic pain.*

Special issue on microglia and chronic pain.
Hulsebosch CE
Exp Neurol. 2012 Jan 17. [Epub ahead of print]

This special issue of Experimental Neurology is devoted to the role of Microglia and Chronic Pain. Chronic pain affects 116 million people per year in the United States, which is more than heart disease, cancer, and diabetes combined. Nervous system trauma and disease are principal contributors to the establishment of chronic pain in people and in animal models. Central nervous system (CNS) injury or tumor development, peripheral nerve injury, multiple sclerosis, diabetes and many other neurological disruptions can serve as the instigating pathophysiolgical conditions that lead to chronic pain. Once considered to function solely as the phagocytotic cells of the CNS, more recent work has demonstrated that persistent activation of the microglial population may contribute to continued dysfunction including chronic pain. In the invited articles for this special issue on Microglia and Chronic Pain, we present evidence for the role of persistent microglial activation in chronic pain after peripheral and central nervous system injury, as well as in diabetic pain, post-herpetic neuralgia pain and related diseases. Collectively, the body of work indicates the importance of understanding the roles of microglial cells in chronic pain which will lead to targeted treatment to attenuate or alleviate chronic neuropathic pain syndromes.

Vulvovaginal Disorders

Developing an interdisciplinary consultation service for vulvar disorders.
Anemüller W, Recke A, Altgassen C, Kelling K
J Dtsch Dermatol Ges. 2012 Feb 14. doi: 10.1111/j.1610-0387.2012.07837.x. [Epub ahead of print]

BACKGROUND: Diseases of the vulva often cause severe impairment and long-term problems for the affected women. Adequate treatment requires expert knowledge on the part of treating dermatologists and gynecologists. This was the reason for the initiation of an interdisciplinary consultation service for vulvar diseases at the University Hospital of Lübeck. PATIENTS AND METHODS: Over a period of 2½ years, 208 patients were seen in the new consultation service. Cases were classified as inflammatory diseases, neoplastic diseases, infectious diseases, vulvodynia, or genodermatoses. The effectiveness of treatment was documented by photography, biopsy and - whenever applicable - a quality of life assessment using the Dermatology Life Quality Index (DLQI). RESULTS: Inflammatory dermatoses were diagnosed in 133 patients and neoplas-tic diseases in 32 patients. Infection was diagnosed in 25 patients, vulvodynia in 8, genodermatoses in 3 and other diseases in 7. The DLQI was assessed in 140 patients. Of these, 55 patients had a DLQI > 10 (0-30), indicating severe or extreme impairment of quality of life. A follow-up DLQI was collected in 81 patients, showing a significant improvement. CONCLUSIONS: The patients and both hospital facilities benefitted from the interdisciplinary consultation service. The initial high costs in terms of medical staff and time was compensated by the development of diagnostic and treatment algorithms. Overall, the concept received positive feedback from patients and medical staff members.

Role of vulvar care guidelines in the initial management of vulvar complaints.
Lifits-Podorozhansky YM, Podorozhansky Y, Hoffstetter S, Gavard JA
J Low Genit Tract Dis. 2012 Apr;16(2):88-91.

OBJECTIVE: This study aimed to determine the effectiveness of vulvar care guidelines as the initial treatment of vulvar complaints. MATERIALS AND METHODS: A chart review was conducted at the Saint Louis University Vulvar and Vaginal Disease Center. Women with vulvar symptoms in the absence of specific identifiable causes were evaluated and given guidelines for vulvar care. An 11-point Likert scale was used to rate symptoms at the initial and follow-up visits. Compliance level was determined. RESULTS: A decrease in mean scores was shown for dyspareunia (7.5 ± 2.0 to 4.6 ± 3.1, $p < .001$), burning after intercourse (6.8 ± 2.7 to 3.4 ± 2.4, $p = .10$), vulvar burning (5.7 ± 2.6 to 2.1 ± 1.9, $p < .001$), vulvar itching (4.9 ± 2.8 to 2.5 ± 2.6, $p < .001$), and vulvar pain (5.8 ± 2.8 to 2.2 ± 3.0, $p < .01$). The mean dyspareunia difference scores were significant between the low- and high-compliance groups. CONCLUSIONS: Vulvar care guidelines are successful for the management of vulvar complaints.

Cytology of the vulva: feasibility and preliminary results of a new brush.
van den Einden LC, Grefte JM, van der Avoort IA, Vedder JE, van Kempen LC, Massuger LF, de Hullu JA
Br J Cancer. 2012 Jan 17;106(2):269-73. doi: 10.1038/bjc.2011.533. Epub 2011 Dec 1.

OBJECTIVE: Taking a biopsy is a standard procedure to make the correct diagnosis in patients with suspicious premalignant vulvar lesions. The use of a less invasive diagnostic tool as triage instrument to determine whether biopsy is necessary may improve patient comfort especially in patients with chronic vulvar disorders that may warrant consecutive biopsies. This study was conducted to investigate whether vulvar brush cytology is feasible and may be used to detect (pre)malignant vulvar lesions. METHODS: A pilot study was performed with patients having clinically normal vulvar skin, lichen sclerosus (LS), usual or differentiated vulvar intraepithelial neoplasia or squamous cell carcinoma. A total of 65 smears were taken with the use of a vulvar brush and biopsies were performed for histopathological analysis. RESULTS: Out of 65 smears, 17 (26%) were discarded because of poor cellularity. A total of 28 of 29 (97%) smears with a histological proven (pre)malignancy had a smear classified as 'suspicious' or 'uncertain'.

Cytology classified 11 smears as 'non-suspicious', of which 10 (91%) were indeed normal skin or LS. The accuracy, based on the presence of a lesion, for (pre)malignant lesions with the use of the brush showed a sensitivity of 97% and a negative predictive value of 88%. CONCLUSION: Vulvar brush cytology is feasible and may be a first step in the development of a triage instrument to determine whether subsequent biopsy of a clinically (pre)malignant lesion is necessary.

A multicenter study of the clinical characteristics of usual-type vulvar intraepithelial neoplasia in China.
Li X, Zhu L, Gu Y, Jin H, Wang C, Lang J
Int J Gynaecol Obstet. 2012 Jan 17. [Epub ahead of print]

OBJECTIVE: To investigate clinical characteristics of usual-type vulvar intraepithelial neoplasia (uVIN) in China. METHODS: A retrospective review of the records of 64 patients with uVIN was performed at 3 academic hospitals between 2004 and 2010. Patients were assigned to a younger (≤40years) or an older (>40years) group. Clinical characteristics of lesions were described and analyzed. RESULTS: Mean patient age was 40.6 years. There was a high proportion of incidental findings (34%), multifocal lesions (64%), variegated lesions (59%), and multiple neoplastic lesions in the lower genital tract (20%). As patient age increased, so did numbers of patients reporting pain ($P<0.05$). Longer time between symptom onset and uVIN diagnosis, and more multifocal lesions were noted in the older group ($P<0.05$). Whereas younger patients often presented with cervical intraepithelial neoplasia and uVIN, older patients often presented with intraepithelial neoplasia at uncommon locations (e.g. vagina, anus, and periurethral region) ($P<0.05$). No differences between the groups were found regarding gross appearance or anatomic location of uVIN lesions ($P>0.05$). CONCLUSION: Age-specific differences were noted in location of neoplastic lesions in the lower genital tract and time to diagnosis of uVIN. However, the clinical features of uVIN lesions were heterogeneous and non-age specific.

Rapid spontaneous regression of acute-onset vulvar intraepithelial neoplasia 3 in young women: a case series.
Stephenson RD, Denehy TR
J Low Genit Tract Dis. 2012 Jan;16(1):56-8.

OBJECTIVE: Vulvar intraepithelial neoplasia 3 (VIN 3)/vulvar carcinoma in situ is currently treated by surgical excision, laser ablation, or topically with 5-fluorouracil or imiquimod. The rate of progression of untreated VIN 3/vulvar carcinoma in situ to invasive cancer is significant, although difficult to assess, because most patients undergo treatment. The peak incidence of invasive carcinoma of the vulva occurs in the sixth decade, which may indicate that human papillomavirus (HPV)-related preinvasive disease in the younger population has a lower progression rate. However, the risk of invasive disease cannot be disregarded. METHODS: This is a case series of complete spontaneous resolution of untreated VIN 3/vulvar carcinoma in situ in 5 healthy women aged 20 to 36 years from a single community gynecologic oncologist practice from 2006 to 2010. RESULTS: Complete spontaneous regression of acute VIN 3/vulvar carcinoma in situ was reported in 6 healthy young women aged 20 to 36 years. New sexual partners were reported in 2 of the 6 patients preceding the onset of vulvar lesions within 6 months. All patients were nonsmokers, healthy without known immunocompromise, and noted the acute onset of vulvar lesions. Vulvar intraepithelial neoplasia 3/vulvar carcinoma in situ was diagnosed on biopsy and confirmed on independent review. All lesions were multifocal in nature. Time to spontaneous regression was 6, 6, 8, 12, 18, and 20 weeks after initial biopsy. No patient received the HPV vaccine. Recurrence has not been noted in any of the patients within the follow-up period of 6 to 60 months. CONCLUSIONS: Short-term follow-up with conservative management of acute-onset VIN 3/vulvar carcinoma in situ in this young patient population correlates with similar treatment strategies for HPV-related cervical intraepithelial neoplasia of the cervix and may prevent disfigurement, pain, and complications associated with the current recommended therapeutic modalities. The timing of intervention for VIN 3/vulvar carcinoma in situ in the young population needs clarification. Future studies are in order.

A phase II trial of radiation therapy and weekly cisplatin chemotherapy for the treatment of locally-advanced squamous cell carcinoma of the vulva: A gynecologic oncology group study.
Moore DH, Ali S, Koh WJ, Michael H, Barnes MN, McCourt CK, Homesley HD, Walker JL
Gynecol Oncol. 2012 Mar;124(3):529-33.

OBJECTIVES: To determine the efficacy and toxicity of radiation therapy and concurrent weekly cisplatin chemotherapy in achieving a complete clinical and pathologic response when used for the primary treatment of locally-advanced vulvar carcinoma. METHODS: Patients with locally-advanced (T3 or T4 tumors not amenable to surgical resection via radical vulvectomy), previously untreated squamous cell carcinoma of the vulva were treated with radiation (1.8Gy daily×32 fractions=57.6Gy) plus weekly cisplatin (40mg/m(2)) followed by surgical resection of residual tumor (or biopsy to confirm complete clinical response). Management of the groin lymph nodes was standardized and was not a statistical endpoint. Primary endpoints were complete clinical and pathologic response rates of the primary vulvar tumor. RESULTS: A planned interim analysis indicated sufficient activity to reopen the study to a second stage of accrual. Among 58 evaluable patients, there were 40 (69%) who completed study treatment. Reasons for prematurely discontinuing treatment included: patient refusal (N=4), toxicity (N=9), death (N=2), other (N=3). There were 37 patients with a complete clinical response (37/58; 64%). Among these women there were 34 who underwent surgical biopsy and 29 (78%) who also had a complete pathological response. Common adverse effects included leukopenia, pain, radiation dermatitis, pain, or metabolic changes. CONCLUSIONS: This combination of radiation therapy plus weekly cisplatin successfully yielded high complete clinical and pathologic response rates with acceptable toxicity.

Local fasciocutaneous infragluteal (FCI) flap for vulvar and vaginal reconstruction: a new technique in cancer surgery.
Windhofer C, Papp C, Staudach A, Michlits W
Int J Gynecol Cancer. 2012 Jan;22(1):132-8.

INTRODUCTION: Soft tissue reconstruction after vulvar, vaginal, or anal cancer resection poses a formidable task for reconstructive surgeons because of the functional, locational, and cosmetic importance of this region. Although numerous flaps have been designed for vulvar reconstruction, each has its disadvantages. METHODS: The authors introduce the local fasciocutaneous infragluteal (FCI) flap for vulvar and vaginal reconstruction after tumor resection, vaginal scar obliteration, and vulvar ulceration in 15 patients operated on between 1999 and 2007. The FCI flap is supplied by the cutaneous branch of the descending branch of the inferior gluteal artery. The sensory supply of this flap comes from side branches of the posterior cutaneous nerve of the thigh. A total of 17 flaps were performed in 15 patients. RESULTS: Except for one, all flaps survived. One flap necrosis occurred because of false postoperative position with compression and tension to the vascular pedicle. In the remaining patients, we found one local cancer recurrence with necessity of a second flap from the contralateral side. The patients report satisfaction with reconstruction, without one having pain at donor site and recurrent vaginal ulceration. CONCLUSIONS: This article discusses the expanding indications of this versatile flap and the operative technique of the local FCI flap for reconstruction of vulvar and partial vaginal defects. It can be raised in different volume and dimension out of possible irradiated area with an inconspicuous scar.

Gastrointestinal stromal tumor presenting as dyspareunia.
Kamali S, Akan A, Aydin T, Karatepe O, Kamali G, Adaş G
Turk J Gastroenterol. 2011 Oct;22(5):558-9.

No abstract available.

Paget's disease of the vulva with bladder invasion: a case report.
Inoue S, Shiina H, Igawa M
Arch Gynecol Obstet. 2011 Nov 24. [Epub ahead of print]

Tumor excision and dermal-flap skin graft operations were performed on a 72-year-old woman diagnosed with extramammary Paget's disease at our hospital in August 2001. Paget cells were identified in the external urethral meatus even though nine local excisions of recurrent tumors had been performed. She was suffered from severe vesical pain from May 2007. Urine cytology was class V and physical examination revealed redness in external urethral meatus. Pelvic MRI did not show apparent lymph node swelling and the endoscopic multiple biopsies performed at multiple bladder mucosa and distal urethra. Pathological diagnosis of the endoscopic biopsy showed multiple Paget cells from urethra, posterior and bilateral lateral wall, and bladder neck. Because Paget's disease may infiltrate bladder mucosa and cause severe vesical pain due to bladder invasion, total cystorethrectomy, ileal conduit, and external skin excision were performed. Pathological findings were continuous infiltration of Paget cells from external urethral meatus to bladder mucosa.

Benign vulvar dermatoses.
Rodriguez MI, Leclair CM
Obstet Gynecol Surv. 2012 Jan;67(1):55-63.

Vulvar pruritus and pain are common indications for consultation with a gynecologist. Contact dermatitis, lichen sclerosus, lichen planus, and vulvar intraepithelial neoplasia are vulvar dermatoses that are often associated with both pruritus and pain. Because these skin conditions are frequently misdiagnosed by providers and incorrectly self-treated by patients, vulvar biopsy is considered the gold standard for diagnosis. The etiology of these vulvar skin conditions is multifactorial; therefore, patient education, behavior modification, and regular follow-up with an experienced clinician are essential to ensure effective control of patient symptoms and management of the skin condition. TARGET AUDIENCE: Obstetricians & Gynecologists and Family Physicians. LEARNING OBJECTIVES: After completing this CME activity physicians should be better able to evaluate common vulvar skin conditions and identify these conditions as a source of significant morbidity for women, diagnose vulvar dermatoses using vulvar biopsy as the gold standard, create a differential diagnosis of vulvar skin disorders.

Interventions for erosive lichen planus affecting mucosal sites.
Cheng S, Kirtschig G, Cooper S, Thornhill M, Leonardi-Bee J, Murphy R
Cochrane Database Syst Rev. 2012 Feb 15;2:CD008092.

BACKGROUND: Erosive lichen planus (ELP) affecting mucosal surfaces is a chronic autoimmune disease of unknown aetiology. It is often more painful and debilitating than the non-erosive types of lichen planus. Treatment is difficult and aimed at palliation rather than cure. Several topical and systemic agents have been used with varying results. OBJECTIVES: To assess the effects of interventions in the treatment of erosive lichen planus affecting the oral, anogenital, and oesophageal regions. SEARCH METHODS: We searched the following databases up to September 2009: the Cochrane Skin Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE (from 2005), EMBASE (from 2007), and LILACS (from 1982). We also searched reference lists of articles and online trials registries for ongoing trials. SELECTION CRITERIA: We considered all randomised controlled trials (RCTs) that evaluated the effectiveness of any topical or systemic interventions for ELP affecting either the mouth, genital region, or both areas, in participants of any age, gender, or race. DATA COLLECTION AND ANALYSIS: The primary outcome measures were as follows:(a) Pain reduction using a visual analogue scale rated by participants; (b) Physician Global Assessment; and (c) Participant global self-assessment.Changes in scores at the end of therapy compared with baseline were analysed. MAIN RESULTS: A total of 15 RCTs were identified, giving a total of 473 participants with ELP. All studies involved oral ELP only. Six of the 15 studies included participants with non-erosive lichen planus. In these studies, only the erosive subgroup was included for intended subgroup analysis. We were unable to pool data from any

of the nine studies with only ELP participants or any of the six studies with the ELP subgroup, due to small numbers and the heterogeneity of the interventions, design methods, and outcome variables between studies. One small study involving 50 participants found that 0.025% clobetasol propionate administered as liquid microspheres significantly reduced pain compared to ointment (Mean difference (MD) -18.30, 95% confidence interval (CI) -28.57 to -8.03), but outcome data was only available in 45 participants. However, in another study, a significant difference in pain was seen in the small subgroup of 11 ELP participants, favouring ciclosporin solution over 0.1% triamcinolone acetonide in orabase (MD -1.40, 95% CI -1.86 to -0.94). Aloe vera gel was 6 times more likely to result in at least a 50% improvement in pain symptoms compared to placebo in a study involving 45 ELP participants (Risk ratio (RR) 6.16, 95% CI 2.35 to 16.13). In a study involving 20 ELP participants, 1% pimecrolimus cream was 7 times more likely to result in a strong improvement as rated by the Physician Global Assessment when compared to vehicle cream (RR 7.00, 95% CI 1.04 to 46.95). There is no overwhelming evidence for the efficacy of a single treatment, including topical steroids, which are the widely accepted first-line therapy for ELP. Several side-effects were reported, but none were serious. With topical corticosteroids, the main side-effects were oral candidiasis and dyspepsia. AUTHORS' CONCLUSIONS: This review suggests that there is only weak evidence for the effectiveness of any of the treatments for oral ELP, whilst no evidence was found for genital ELP. More RCTs on a larger scale are needed in the oral and genital ELP populations. We suggest that future studies should have standardised outcome variables that are clinically important to affected individuals. We recommend the measurement of a clinical severity score and a participant-rated symptom score using agreed and validated severity scoring tools. We also recommend the development of a validated combined severity scoring tool for both oral and genital populations.

Promoter hypermethylation of death-associated protein kinase and p16 genes in vulvar lichen sclerosus.
Aidé S, Lattario FR, Almeida G, do Val IC, Carvalho Mda G
J Low Genit Tract Dis. 2012 Apr;16(2):133-9.

OBJECTIVE: The purpose of this study was to discuss our investigation of the hypermethylation of promoter regions of tumor suppressor genes, such as death-associated protein kinase (DAPK) and p16, in vulvar lichen sclerosus (LS), in comparison with a control group. MATERIALS AND METHODS: Promoter hypermethylation of DAPK and p16 was investigated using 24 vulvar biopsies of patients with LS who had received no previous treatment. The control group was composed of 15 patients with no vulvar disease. The DNA of subjects was treated with sodium bisulphate, and the genes under study were subjected to methylation-specific polymerase chain reaction. The resulting polymerase chain reaction products were amplified and analyzed using a 10% polyacrylamide gel. RESULTS: The mean age of the patients with LS was 57 years (the majority were postmenopausal). In the control group, the mean age of the patients was 50 years (p = .151). Methylation of the promoter region of DAPK was found in 4 (17%) of the 23 patients analyzed, and p16 promoter region methylation was found in 8 patients (35%). Two cases of methylation of the DAPK gene were also found to be methylated for the p16 gene. In the control group, no methylation was found in the patients analyzed for the DAPK gene and methylation was found in 3 (21%) of the 14 patients analyzed for the p16 gene (p = .190 and p = .316, respectively). CONCLUSIONS**:** Methylation of the DAPK and p16 genes, although not sufficient to dictate prognosis of the disease, should not be underestimated because it may form part of a process of genetic and epigenetic alterations that in the future could become relevant to malignant transformation.

Topical interventions for genital lichen sclerosus.
Chi CC, Kirtschig G, Baldo M, Brackenbury F, Lewis F, Wojnarowska F
Cochrane Database Syst Rev. 2011 Dec 7;12:CD008240.

BACKGROUND: Lichen sclerosus is a chronic, inflammatory skin condition that most commonly occurs in adult women, although it may also be seen in men and children. It primarily affects the genital area and around the anus, where it causes persistent itching and soreness. Scarring after inflammation may lead to severe damage by fusion of the vulval lips (labia); narrowing of the vaginal opening; and burying of the clitoris in women and girls, as well as tightening of the foreskin in men and boys, if treatments are not started early. Affected people have an increased risk of genital cancers.

OBJECTIVES: To assess the effects of topical interventions for genital lichen sclerosus and adverse effects reported in included trials. SEARCH METHODS**:** We searched the following databases up to 16 September 2011: the Cochrane Skin Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE (from 2005), EMBASE (from 2007), LILACS (from 1982), CINAHL (from 1981), British Nursing Index and Archive (from 1985), Science Citation Index Expanded (from 1945), BIOSIS Previews (from 1926), Conference Papers Index (from 1982), and Conference Proceedings Citation Index - Science (from 1990). We also searched ongoing trial registries and scanned the bibliographies of included studies, published reviews, and papers that had cited the included studies. SELECTION CRITERIA: Randomised controlled trials (RCTs) of topical interventions in genital lichen sclerosus. DATA COLLECTION AND ANALYSIS: Two authors independently selected trials, extracted data, and assessed the risk of bias. A third author was available for resolving differences of opinion. MAIN RESULTS: We included 7 RCTs, with a total of 249 participants, covering 6 treatments. Six of these RCTs tested the efficacy of one active intervention against placebo or another active intervention, while the other trial tested three active interventions against placebo. When compared to placebo in one trial, clobetasol propionate 0.05% was effective in treating genital lichen sclerosus in relation to the following outcomes: 'participant-rated improvement or remission of symptoms' (risk ratio (RR) 2.85, 95% confidence interval (CI) 1.45 to 5.61) and 'investigator-rated global degree of improvement' (standardised mean difference (SMD) 5.74, 95% CI 4.26 to 7.23). When mometasone furoate 0.05% was compared to placebo in another trial, there was a significant improvement in the 'investigator-rated change in clinical grade of phimosis' (SMD -1.04, 95% CI -1.77 to -0.31). Both trials found no significant differences in reported adverse drug reactions between the corticosteroid and placebo groups. The data from four trials found no significant benefit for topical testosterone, dihydrotestosterone, and progesterone. When used as maintenance therapy after an initial treatment with topical clobetasol propionate in another trial, topical testosterone worsened the symptoms ($P < 0.05$), but the placebo did not. One trial found no differences between pimecrolimus and clobetasol propionate in relieving symptoms through change in pruritus (itching) (SMD -0.33, 95% CI -0.99 to 0.33) and burning/pain (SMD 0.03, 95% CI -0.62 to 0.69). However, pimecrolimus was less effective than clobetasol propionate with regard to the 'investigator-rated global degree of improvement' (SMD -1.64, 95% CI -2.40 to -0.87). This trial found no significant differences in reported adverse drug reactions between the pimecrolimus and placebo groups. AUTHORS' CONCLUSIONS: The current limited evidence demonstrates the efficacy of clobetasol propionate, mometasone furoate, and pimecrolimus in treating genital lichen sclerosus. Further RCTs are needed to determine the optimal potency and regimen of topical corticosteroids, examine other topical interventions, assess the duration of remission or prevention of flares, evaluate the reduction in the risk of genital squamous cell carcinoma or genital intraepithelial neoplasia, and examine the efficacy in improving the quality of the sex lives of people with this condition.

A population-based case-control study of aetiological factors associated with vulval lichen sclerosus.

Higgins CA, Cruickshank ME

J Obstet Gynaecol. 2012 Apr;32(3):271-5.

We aimed to investigate the association between possible aetiological factors and the risk of developing vulval lichen sclerosus (VLS). A population-based case-control questionnaire study was performed comparing women with a diagnosis of VLS (n= 92), with those attending a general gynaecology clinic with no known anogenital dermatosis (n= 66). After adjustment for confounders, factors associated with VLS included a family history of diabetes mellitus (OR= 7.0, p= 0.012) and previous pelvic surgery (OR= 4.75, p= 0.007). The use of barrier and progesterone only methods of contraception (OR= 0.19, p= 0.045), hormone replacement therapy (OR= 0.209, p= 0.025) or hayfever (OR= 0.18, p = 0.008) appeared to be associated with a reduced risk of VLS. In conclusion, we were unable to confirm many proposed aetiological theories associated with the development of VLS, in particular those associated with autoimmunity.

The co-existence of vulvar lichen sclerosus, ulcerated calcinosis cutis, and dermatomyositis: coincidence or immunological mechanism?
Balcı DD, Celik E, Sarıkaya G, Yenin JZ, Atik E
Ann Dermatol. 2011 Dec;23(Suppl 3):S375-9.

Calcinosis cutis is a condition characterized by the deposition of calcium salts in the skin and subcutaneous tissues, and patients suffering from it encounter various connective tissue disorders, such as dermatomyositis (DM), scleroderma, and systemic lupus erythematosus. Although calcinosis cutis is frequently accompanied by juvenile dermatomyositis, rare cases have been reported in adult patients with DM. On the other hand, lichen sclerosus (LS) is a chronic inflammatory disease of the skin and mucosal surfaces. In the present report, we present a rare case of a 71-year-old patient with DM accompanied by ulcerated calcinosis cutis and vulvar LS.

Differential expression of connective tissue growth factor and extracellular matrix proteins in lichen sclerosus.
Gambichler T, Skrygan M, Czempiel V, Tigges C, Kobus S, Meier JJ, Köhler CU, Scola N, Stücker M, Altmeyer P, Kreuter A
J Eur Acad Dermatol Venereol. 2012 Feb;26(2):207-12. doi: 10.1111/j.1468-3083.2011.04037.x.

BACKGROUND: The histopathology of lichen sclerosus (LS) suggests abnormalities in extracellular matrix (ECM) composition. OBJECTIVES: We aimed to investigate the expression pattern of ECM proteins and related growths factors and Smad signal transducers in LS as compared with healthy skin. METHODS: To assess the expression of decorin, biglycan, versican, perlecan, fibronectin, dermatopontin, extracellular matrix protein 1 (ECM-1), matrix metalloproteinase 1, tissue inhibitor of metalloproteinase 1, connective tissue growth factor (CTGF), transforming growth factor β1, and Smad-3 protein, real-time RT-PCR and immunohistochemistry were performed on skin specimens obtained from the genital region of healthy subjects (n = 10) as well as LS patients (n = 26). RESULTS: Median mRNA as well as mean protein expression of biglycan, versican, fibronectin, and ECM-1 was significantly higher in LS when compared with healthy controls. Both mRNA and protein CTGF expression observed in LS was significantly higher than in controls. CTGF mRNA expression significantly correlated with mRNA expression of biglycan, versican and fibronectin. CONCLUSIONS: Expression of ECM proteins (e.g. proteoglycans, ECM-1) and CTGF is altered in LS. TGF-ß/Smad-3 independent up-regulation of CTGF may induce accumulation of ECM proteins and maintain fibrosis in chronic LS.

Lichen Sclerosus: A 5-year follow-up after topical, subdermal, or combined therapy.
Ventolini G, Swenson KM, Galloway ML
J Low Genit Tract Dis. 2012 Jan 17. [Epub ahead of print]

OBJECTIVE: The purpose of our study was to compare clinical data regarding patients with pruritic lichen sclerosus (LS) at moderate or severe stages using 2 different therapies with a 5-year follow-up. MATERIALS AND METHODS: The study was approved by the institutional review board and was presented as a retrospective clinical data review of patients with pruritic biopsy diagnosis LS who underwent therapy at our university private practice from 2002 to 2005. We compared the results of a weekly topical application of high-potency steroid (HPS) with a combined HPS and monthly anesthetic/steroid subdermal injection (ASI). Outcomes were timed to achieve pruritus-free status, the number of symptomatic recurrences, and patient satisfaction with therapy. RESULTS: Fifty-four patients were diagnosed with LS between 2002 and 2005. There were 13 patients who had mild-stage, 25 who had moderate-stage, and 16 who had severe-stage LS. Five-year follow-up data on 17 patients with moderate-stage LS and 14 patients with severe-stage LS were obtained. Time to pruritus free was 6 weeks with ASI and 19 weeks with HPS for moderate-stage LS ($p = .04$) and 9 weeks with ASI and 24 weeks with HPS for severe-stage LS ($p = .03$). Recurrences were more frequent on HPS for moderate-stage LS ($p = .04$) but not significant with HPS for severe-stage LS ($p = .15$). Only ASI was successful at treating patients with recalcitrant pruritus. CONCLUSIONS: In our population, patients with symptomatic moderate-stage LS seem to have a more rapid and prolonged response to ASI than to HPS but are less satisfied with the injections.

Metalloproteinases 2 and 9 and their tissue inhibitors 1 and 2 are increased in vulvar lichen sclerosus.
De Oliveira GA, de Almeida MP, Soares FA, de Almeida Filho GL, Takiya CM, Otazu IB, Nasciutti LE
Eur J Obstet Gynecol Reprod Biol. 2011 Dec 24. [Epub ahead of print]

OBJECTIVES: To evaluate the expression of different matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) in vulvar lichen sclerosus (LS), a chronic dermatosis in women, histologically characterized by a zone of collagen remodeling in the superior dermis. STUDY DESIGN: Analysis of the expression of different MMPs (MMP-1, -2, -9 and -13) and TIMPs (TIMP-1 and -2) by reverse transcriptase-polymerase chain reaction (RT-PCR) in vulvar biopsies from patients with LS (n=11), classified according to Hewitt histological criteria and compared with clinically normal vulvar tissue (n=5), and the immunohistochemistry of MMP-2 and -9 and TIMP-1 and -2 distribution in the remodeling zone of LS (n=31) and in clinically normal vulvar tissue (n=28). RESULTS: Although no statistically significant difference between LS and normal skin groups at the mRNA level of MMP and TIMP transcripts was shown, an increase in the immunodistribution of MMP-2 and -9 and TIMP-1 and -2 in LS compared to normal vulvar skin was observed. CONCLUSIONS: These results suggest that these molecules could be related to the process of cutaneous collagen remodeling in LS pathology.

The surgical management of complications of vulval lichen sclerosus.
Gurumurthy M, Morah N, Gioffre G, Cruickshank ME
Eur J Obstet Gynecol Reprod Biol. 2012 Mar 5.

OBJECTIVE: To review the surgical procedures used to treat the complications of vulval lichen sclerosus at a single tertiary referral institution in north-east Scotland over a ten year period. STUDY DESIGN: A retrospective case note review of women who had surgery for ano-genital lichen sclerosus at Aberdeen Royal Infirmary between January 1999 and December 2009. RESULTS: The total number of women was 25 and the two most common procedures were Fenton's procedure (median perineotomy) and laser division of adhesions. Initial surgery resulted in an improvement of symptoms for 80% of women. CONCLUSIONS: When surgery for vulval lichen sclerosus is reserved for highly selected cases where there are complications secondary to adhesions, the proportion of women benefiting is high.

Vulvar inflammatory dermatoses.
Barchino-Ortiz L, Suárez-Fernández R, Lázaro-Ochaita P
Actas Dermosifiliogr. 2011 Dec 15. [Epub ahead of print]

Vulvar skin disease is a common reason for consultation. The vulva, like the rest of the skin, can be affected by numerous diseases of various etiologies, but its particular anatomic and physiologic characteristics create additional diagnostic and therapeutic difficulties. The study of vulvar disease is emerging as a new branch of dermatology. In this article, we examine the characteristics of the normal vulva, and perform a brief, structured review of vulvar inflammatory dermatoses, which comprise a heterogeneous group of diseases in which a broad, multidisciplinary approach is essential.

An autoimmune phenotype in vulvar lichen sclerosus and lichen planus: A Th1 response and high levels of microRNA-155.
Terlou A, Santegoets LA, van der Meijden WI, Heijmans-Antonissen C, Swagemakers SM, van der Spek PJ, Ewing PC, van Beurden M, Helmerhorst TJ, Blok LJ
J Invest Dermatol. 2012 Mar;132(3):658-66. doi: 10.1038/jid.2011.369.

Vulvar lichen sclerosus and lichen planus are T-cell-mediated chronic skin disorders. Although autoimmunity has been suggested, the exact pathogenesis of these disorders is still unknown. Therefore, the aim of the current study was to investigate the molecular and immunological mechanisms critical to the pathogenesis of vulvar lichen sclerosus and

lichen planus. By using gene expression profiling and real-time RT-PCR experiments, we demonstrated a significantly increased expression of the pro-inflammatory cytokines (IFNγ, CXCR3, CXCL9, CXCL10, CXCL11, CCR5, CCL4, and CCL5) specific for a Th1 IFNγ-induced immune response. In addition, BIC/microRNA-155 (miR-155)-a microRNA involved in regulation of the immune response-was significantly upregulated in lichen sclerosus and lichen planus (9.5- and 17.7-fold change, respectively). Immunohistochemistry showed a significant T-cell response, with pronounced dermal infiltrates of CD4(+), CD8(+), and FOXP3(+) cells. In conclusion, these data demonstrate an autoimmune phenotype in vulvar lichen sclerosus and lichen planus, characterized by increased levels of Th1-specific cytokines, a dense T-cell infiltrate, and enhanced BIC/miR-155 expression.

Clitoral neuroma after female genital mutilation/cutting: A rare but possible event.
Abdulcadir J, Pusztaszeri M, Vilarino R, Dubuisson JB, Vlastos AT
J Sex Med. 2011 Dec 6. doi: 10.1111/j.1743-6109.2011.02558.x. [Epub ahead of print]

INTRODUCTION: Female genital mutilation/cutting (FGM/C), in particular, type III, also called infibulation, can cause various long-term complications. However, posttraumatic neuroma of the clitoris is extremely rare; only one case was previously reported in the literature. AIM: The aim of this study was to describe the case of a patient presenting a clitoral neuroma post-FGM/C in detail and her successful multidisciplinary treatment. METHODS: We report the case of a 24-year-old woman originating from Somalia presenting a type III a-b FGM/C who attended our outpatient clinic at the Geneva University Hospitals complaining of primary dysmenorrhea and a post-mutilation painful clitoral mass. The mass was clinically diagnosed as a cyst and surgically removed. Histopathological analysis revealed that it was a posttraumatic neuroma and a foreign body granuloma around the ancient surgical thread. Our patient was also offered a multidisciplinary counseling by a specialized gynecologist on FGM/C, a sexologist, and a reproductive and sexual health counselor. RESULTS: One month after surgical treatment, the vulvar pain was over. CONCLUSIONS: This is the second case of clitoral neuroma after FGM/C reported and the first with complete clinical, as well as histopathological documentation and multidisciplinary care. Considering the high frequency of clitoral cysts in case of infibulation, clitoral neuroma should be considered in the differential diagnosis. In this case, if symptomatic, the treatment should be surgery, clinical follow-up, and counseling. If necessary, appropriate sexual therapy should be offered too.

Clinical effects of treatment with phytoestrogens in postmenopausal women. [Article in Italian]
Ciotta L, Stracquadanio M, Pagano I, Andò A, Valenti O, Roccasalva L
Minerva Ginecol. 2012 Feb;64(1):15-22.

AIM AND METHODS: Phytoestrogens are plant substances that have estrogenic properties; they haven't steroid structure but they are heterocyclic phenols and for this reason are similar to 17 β estradiol from the functional and structural point of view; they compete for the same receptor sites of endogenous estrogens, but with an activating capacity a thousand times lower. For this reason, the isoflavones are an alternative to hormone-replacement treatment: they are prescribed to all those women who cannot be treated with HRT for several contraindications, such as thrombosis or breast tumor familiarity. The aim of our study was to demonstrate the effectiveness of soy isoflavones on menopausal symptoms. RESULTS AND CONCLUSION: In our experience, literature data were confirmed, with a 40% reduction of the vasomotor symptoms after 6 months of treatment. Associated with this improvement, there is also the reduction in the degree of insomnia and depressive symptoms. The musculoskeletal pains, however, are not reduced significantly as no positive change was found on vaginal dryness, a major cause of dyspareunia in postmenopausal period.

Comparison of vaginal gel isoflavones versus no topical treatment in vaginal dystrophy: results of a preliminary prospective study.
Tedeschi C, Benvenuti C
Gynecol Endocrinol. 2012 Feb 9. [Epub ahead of print]

OBJECTIVE: Vaginal dystrophy due to hypo-oestrogenism takes advantage of local and systemic oestrogens to balance the vaginal ecosystem and improve tissue hydration. Women who do not accept/tolerate hormone therapy can use intravaginal isoflavones to relieve vaginal dryness. The aim of this study was to investigate the clinical effect of a vaginal gel formulation containing isoflavones compared with no topical treatment in women with vaginal dystrophy. MATERIAL AND METHODS: In a multicentre, controlled, parallel-group study, menopausal women with vaginal dystrophy were randomized to vaginal gel (EG) or no topical treatment (NT) for 4 weeks. EG contained isoflavones, Lactobacillus sporogenes, Calendula officinalis extract and lactic acid (Estromineral Gel, Rottapharm-Madaus). All patients received daily oral isoflavones plus L. sporogenes. Clinical evaluations were performed at time 0, 2 and 4 weeks. RESULTS: 186 women were recruited, 103 in the EG group and 83 in the NT group, mean age 53.7 years, postmenopausal for 4.1 years. The severity of itching, burning, vulvovaginal erythema, vaginal dryness and dyspareunia were significantly reduced during EG treatment compared with the NT group. CONCLUSIONS: The combination of oral and topical isoflavones was shown to be more effective than oral treatment alone in reducing the problems of postmenopausal vaginal dystrophy.

Efficacy of the Mentha crispa in the treatment of women with Trichomonas vaginalis infection.
Moraes ME, Cunha GH, Bezerra MM, Fechine FV, Pontes AV, Andrade WS, Frota Bezerra FA, Moraes MO, Cavalcanti PP
Arch Gynecol Obstet. 2012 Feb 21. [Epub ahead of print]

PURPOSE: The aim of this study was to evaluate the efficacy of Mentha crispa in the treatment of women with Trichomonas vaginalis infection (TVI). METHODS: This was a randomized, double-blind, and controlled clinical trial consisting of three phases, pre-treatment, treatment, and post-treatment. Sixty female patients were randomized to a treatment group, M. crispa (24 mg) or secnidazole (2,000 mg), both consisting of single dose. RESULTS: After treatment the proportion of patients without TVI in secnidazole group was 96.6% and in the M. crispa group was 90%, no difference was found between groups ($P = 0.6120$). We observed improvement in vaginal discharge, malodorous vaginal secretion, dyspareunia, dysuria, pelvic pain, and burning and itching in the genital area in patients of both groups of treatment, with no statistically significant differences between them ($P > 0.05$). Adverse effects were significantly higher ($P = 0.0006$) in the secnidazole group (66.6%) than in the M. crispa group (20%), that being mostly nausea and metallic taste with statistically significant differences between treatment groups ($P < 0.001$). CONCLUSION: This study is the first to show that M. crispa is effective and safe, representing an alternative for the treatment of TVI in women.

Microbiological aspects of vulvovaginitis in prepubertal girls.
Ranđelović G, Mladenović V, Ristić L, Otašević S, Branković S, Mladenović-Antić S, Bogdanović M, Bogdanović D
Eur J Pediatr. 2012 Mar 1. [Epub ahead of print]

This study aimed to establish the vaginal introitus microbial flora in girls with and without symptoms of vulvovaginitis, and to present the distribution of isolated microorganisms by age groups in girls with vulvovaginitis. We enrolled 500 girls with vulvovaginitis symptoms, aged 2-12 years, referred by their pediatricians for microbiological examination of the vaginal introitus swabs, and 30 age-matched asymptomatic girls. Similar microbial flora was isolated in both groups, but the symptomatic girls had significantly more common positive microbiological findings compared to controls ($p<0.001$). In symptomatic girls, the following pathogenic bacteria were isolated: Streptococcus pyogenes (4.2%), Haemophilus influenzae (0.4%), and Staphylococcus aureus (5.8%). Bacteria of fecal origin were found in vaginal introitus swabs in 33.8% of cases, most commonly Proteus mirabilis (14.4%), Enterococcus faecalis (12.2%), and Escherichia coli (7.0%). The finding of fecal flora was more common compared to controls, reaching a statistical significance ($p<0.05$), as well as in girls aged up to 6 years ($p<0.001$). Candida species were found in 2.4% of girls with vulvovaginitis symptoms. CONCLUSIONS: The microbial ecosystem in girls with clinical signs of vulvovaginitis is complex

and variable, and the presence of a microorganism does not necessarily imply that it is the cause of infection. The diagnosis of vulvovaginitis in prepubertal girls requires a complex and comprehensive approach, and microbiological findings should be interpreted in the context of clinical findings.

Yeast vaginitis during pregnancy: susceptibility testing of 13 antifungal drugs and boric acid and the detection of four virulence factors.
Kalkanci A, Güzel AB, Khalil II, Aydin M, Ilkit M, Kuştimur S
Med Mycol. 2012 Feb 28. [Epub ahead of print]

A higher prevalence of vulvovaginal candidiasis (VVC) is seen in pregnant women compared with those who are not pregnant. Recurrence is also more common in pregnant women, and therapeutic responses are reduced. In this investigation, 207 vaginal yeast isolates recovered from pregnant women were tested for susceptibility to 13 antifungal drugs and boric acid and through these studies four virulence factors were also determined. The isolates were recovered from vaginal samples of patients with acute VVC [AVVC, (n =73)], symptomatic recurrent VVC [RVVC, (n =89)], asymptomatic RVVC (n =27), and those without signs and symptoms (n =18). Candida albicans was the most common species found (59.9%), followed by C. glabrata (19.8%), other Candida spp., (19.8%), and Saccharomyces cerevisiae (0.5%). Antifungal susceptibility testing was performed as described in CLSI document M27-A3. Additionally, we examined phospholipase and proteinase production, adhesion to vaginal epithelial cells and hemolytic activity. Notably, the MIC values of Candida spp. isolates derived from patients with VVC were no different from those of the controls ($P > 0.05$). In addition, Candida isolates derived from patients with AVVC or RVVC produced significantly higher amounts of phospholipase and proteinase compared with the controls ($P < 0.05$). Antifungal testing and the determination of virulence factors may lead to the effective and prompt treatment of VVC, particularly in pregnant women.

Bee-honey and yogurt: a novel mixture for treating patients with vulvovaginal candidiasis during pregnancy.
Abdelmonem AM, Rasheed SM, Mohamed AS
Arch Gynecol Obstet. 2012 Feb 8. [Epub ahead of print]

OBJECTIVE: To evaluate the clinical and mycological cure rates of a novel mixture consisting of Bee-honey and yogurt compared to local antifungal agents for treating patients with vulvo-vaginal candidiasis (VVC) during pregnancy. MATERIALS AND METHODS: This is a prospective comparative study which included 129 patients with VVC during pregnancy. The participants were allocated into study group (n = 82) who received a mixture of Bee-honey and yogurt vaginally and control group (n = 47) who received local anti-fungal agents. The Chi-square test was used to evaluate the clinical and mycological cure rates and the side-effects of both modes of therapy. RESULTS: The clinical cure rate was significantly higher in the study than the control group (87.8 vs. 72.3%, respectively) while the mycological cure rate was higher in the control than the study group (91.5 vs. 76.9%, respectively). Both types of therapy were favorably tolerated by most of the patients. Side effects were reported only in 24.3 and 29.7% of patients in group I and II, respectively ($p < 0.05$). CONCLUSIONS: The mixture of Bee-honey and yogurt produced a high clinical cure rate and a reasonable mycological cure rate. It can be used as a complementary or an alternative to antifungal agents especially in patients with VVC during pregnancy.

The role of cystovaginoscopy and hygienic advice in girls referred for symptoms of vulvovaginitis.
Ram AD, Hurst KV, Steinbrecher H
Arch Dis Child. 2012 Jan 31. [Epub ahead of print]

Vulvovaginitis is a common presenting symptom referred to a paediatric urology clinic. Some of these patients undergo diagnostic cystovaginoscopy to determine whether there is any underlying anatomical cause for the persistent infection. However, in the majority of the patients, no underlying abnormality is found and they are given hygienic advice and prescribed bio yoghurt postoperatively. This study examines the outcome in these patients after hygienic advice is given: determining whether cystovaginoscopy was really necessary and whether it changed the management of vulvovaginitis.

Effect of pH on in vitro susceptibility of Candida glabrata and Candida albicans to 11 antifungal agents and implications for clinical use.

Danby CS, Boikov D, Rautemaa-Richardson R, Sobel JD

Antimicrob Agents Chemother. 2012 Mar;56(3):1403-6.

The treatment of vulvovaginal candidiasis (VVC) due to Candida glabrata is challenging, with limited therapeutic options. Unexplained disappointing clinical efficacy has been reported with systemic and topical azole antifungal agents in spite of in vitro susceptibility. Given that the vaginal pH of patients with VVC is unchanged at 4 to 4.5, we studied the effect of pH on the in vitro activity of 11 antifungal agents against 40 C. glabrata isolates and compared activity against 15 fluconazole-sensitive and 10 reduced-fluconazole-susceptibility C. albicans strains. In vitro susceptibility to flucytosine, fluconazole, voriconazole, posaconazole, itraconazole, ketoconazole, clotrimazole, miconazole, ciclopirox olamine, amphotericin B, and caspofungin was determined using the CLSI method for yeast susceptibility testing. Test media were buffered to pHs of 7, 6, 5, and 4. Under conditions of reduced pH, C. glabrata isolates remained susceptible to caspofungin and flucytosine; however, there was a dramatic increase in the MIC(90) for amphotericin B and every azole drug tested. Although susceptible to other azole drugs tested at pH 7, C. albicans strains with reduced fluconazole susceptibility also demonstrated reduced susceptibility to amphotericin B and all azoles at pH 4. In contrast, fluconazole-sensitive C. albicans isolates remained susceptible at low pH to azoles, in keeping with clinical observations. In selecting agents for treatment of recurrent C. glabrata vaginitis, clinicians should recognize the limitations of in vitro susceptibility testing utilizing pH 7.0.

Protective effect of an oral natural phytonutrient in recurrent vulvovaginal candidiasis: a 12-month study.

Kumari A, Bishier MP, Naito Y, Sharma A, Solimene U, Jain S, Yadava H, Minelli E, Tomella C, Marotta F

J Biol Regul Homeost Agents. 2011 Oct-Dec;25(4):543-51.

The aim of the present study is to assess the clinical efficacy of a phytocompound with antimicotic properties (K-712, with the following 100 mg composition: 10 mg of oleoresin from Pseudowintera colorata at 30 percent concentration in Polygodial together with trace amounts of Olea europea) in recurrent vulvo-vaginal candidiasis (RVVC) as compared to an azole drug during a 12-month period: 6 months of treatment followed by 6 months of observation. This prospective randomized study involved 82 women (19-61 years) with complaints of abnormal vaginal discharge and with a history of at least four proven episodes of RVVC in the previous 12 months. Patients were divided into two groups of treatment of 41 patients each and were given: A) Itraconazole 200 mg orally daily for 4 days, then 200 mg once weekly for 6 months or B) 1 tablet twice a day of a K-712 for 4 weeks and then for the first 2 weeks of each month for a total of 6 months. Both groups were then followed-up for further 6 months. Each treatment schedule was well tolerated with only 4 patients in the azole group complaining of transient mild symptoms (nausea, abdominal discomfort, unpleasant taste). Itraconazole reached an earlier symptomatic relief during the first two weeks of observation as compared with K-712 ($p<0.05$) but both treatments enabled a comparable benefit during the entire treatment study period, afterwards with comparable symptom/sign score (itraconazole vs K-712: 9 vs 11). At 6-month observation, mycological cure was reached by 83 percent in the itraconazole group and in 78 percent of the K-712-treated patients. During the further 6-month observation period without treatment, the itraconazole group showed significantly more relapses (65.7 vs 34.2 in K-712, $p<0.05$) and at the end of the whole 12-month study period the mycological cure was significantly higher in the K-712-treated patients (65.8 vs 34.3 percent, $p<0.05$). There was a non- significant trend increase of less drug-susceptible species in the itraconazole group. From these preliminary data it would appear that a natural antifungal phytocompound proves to be as good as itraconazole in the maintenance treatment of RVVC. Moreover, this approach seems to maintain a higher mycological success rate afterwards by reducing the number of relapses and probably of the growth of azole-resistant species.

Cytokines in the host response to Candida vaginitis: Identifying a role for non-classical immune mediators, S100 alarmins.
Yano J, Noverr MC, Fidel PL Jr
Cytokine. 2012 Apr;58(1):118-28.

Vulvovaginal candidiasis (VVC), caused by Candida albicans, affects a significant number of women during their reproductive years. More than two decades of research have been focused on the mechanisms associated with susceptibility or resistance to symptomatic infection. Adaptive immunity by Th1-type CD4(+) T cells and downstream cytokine responses are considered the predominant host defense mechanisms against mucosal Candida infections. However, numerous clinical and animal studies have indicated no or limited protective role of cells and cytokines of the Th1 or Th2 lineage against vaginal infection. The role for Th17 is only now begun to be investigated in-depth for VVC with results already showing significant controversy. On the other hand, a clinical live-challenge study and an established animal model have shown that a symptomatic condition is intimately associated with the vaginal infiltration of polymorphonuclear leukocytes (PMNs) but with no effect on vaginal fungal burden. Subsequent studies identified S100A8 and S100A9 alarmins as key chemotactic mediators of the acute PMN response. These chemotactic danger signals appear to be secreted by vaginal epithelial cells upon interaction and early adherence of Candida. Thus, instead of a putative immunodeficiency against Candida involving classical immune cells and cytokines of the adaptive response, the pathological inflammation in VVC is now considered a consequence of a non-productive innate response initiated by non-classical immune mediators.

Identification of immune cells by flow cytometry in vaginal lavages from women with vulvovaginitis and normal microflora.
Giraldo PC, de Carvalho JB, do Amaral RL, da Silveira Gonçalves AK, Eleutério J Jr, Guimarães F
Am J Reprod Immunol. 2012 Mar;67(3):198-205. doi: 10.1111/j.1600-0897.2011.01093.x.

PROBLEM: The extent of the vaginal immune response is not fully determined. The purpose of this study was to evaluate the vaginal immune cells from women with vulvovaginitis (VV). METHOD OF STUDY: A total of 142 volunteers diagnosed with bacterial vaginosis (BV), vulvovaginal candidiasis (VC), and BV associated with VC or normal microflora were sampled to evaluate the immune cells by flow cytometry. The immune cells were obtained by vaginal lavage and labeled with fluorochrome-conjugated monoclonal antibodies to identify neutrophil granulocytes, macrophages, CD4(+) and CD8(+) T lymphocytes, B lymphocytes, and NK lymphocytes. RESULTS: Neutrophil granulocytes were present in 84.6% of samples among the leukocyte populations. Considering samples in which neutrophils were present, the mean percentage of neutrophil granulocytes was significantly higher in women with VC than BV and normal microflora and was significantly lower in women with BV than normal microflora. Macrophages and lymphocytes were present in a lower percentage of samples. The mean percentage of CD4(+) T lymphocytes in vaginal lavages was significantly higher in VC and BV compared with women with normal microflora. CONCLUSIONS: Neutrophils were the predominant leukocytes and were associated with VC and inversely with BV. CD4(+) T lymphocytes were associated with both VC and BV.

Recurrent vaginal discharge in children.
McGreal S, Wood P
J Pediatr Adolesc Gynecol. 2012 Jan 19. [Epub ahead of print]

BACKGROUND: Childhood vaginal discharge remains a frequent reason for referral from primary to secondary care. The Paediatric and Adolescent Gynaecology (PAG) service at Kettering General Hospital was established in 1993 and provides a specialized service that meets the needs of children with gynaecological conditions. AIM: To investigate recurrent vaginal discharge noting symptomatology, defining pathogens, common and rarer causes, exploring management regimes, and any changes in practice over time. METHOD: Retrospective review spanning 15 years identifying prepubertal children attending the outpatient PAG clinic with recurrent vaginal discharge. We reviewed the

medical notes individually. RESULTS: 110 patients were identified; 85% were referred from primary care. The age distribution was bimodal at four and eight years. Thirty-five percent of our patients were discharged after the initial consultation. The commonest cause of discharge was vulvovaginitis (82%). Other important causes included suspected sexual abuse (5%), foreign body (3%), labial adhesions (3%), vaginal agenesis (2%). 35% of patients were admitted for vaginoscopy. CONCLUSION: Vaginal discharge is the most common gynecological symptom in prepubertal girls and can cause repeated clinical episodes. Vulvovaginitis is the most common cause and often responds to simple hygiene measures. Awareness of the less common causes of vaginal discharge is essential.

Female genital Chlamydia trachomatis infection: where are we heading?
Mylonas I
Arch Gynecol Obstet. 2012 Feb 19. [Epub ahead of print]

INTRODUCTION: Urogenital infection by Chlamydia trachomatis is the most common bacterial sexually transmitted disease in the world. C. trachomatis is the etiologic agent of several common genital tract syndromes such as urethritis, cervicitis, and pelvic inflammatory disease in women. MATERIALS AND METHODS: In this review, the pathophysiology of a chlamydial infection as well as diagnosis, therapy and prevention strategies regarding female chlamydial infection are reviewed. RESULTS: A chlamydial infection results in minimal or even no symptoms in approximately two-thirds of women, remaining therefore clinically apparent and undiagnosed. C. trachomatis infections are of great socioeconomic and public health concern due to the potential for severe long-term consequences in women, including an increased risk of ectopic pregnancy, tubal infertility and chronic pelvic pain. Moreover, if the bacterium is transmitted during labor to a newborn, it can cause ophthalmia neonatorum and atypical neonatal pneumonia. Due to the documented increased risk of morbidity, several national guidelines are available, including a routine screening for young women and screening during pregnancy that is recommended in several countries. DISCUSSION: A routine screening for young women and screening during pregnancy is recommended in several countries. However, additional prospective studies of the effectiveness of chlamydia screening are warranted and might be feasible within established screening programs. Moreover, the transition from cervicitis to infertility should be also evaluated in future controlled studies to underline the existing evidence. Additionally, there is an urgent need to educate and inform health-care providers about implementation of screening programs to reduce the spread of chlamydial infection. Moreover, awareness and use of screening programs by the public is needed, which requires informational campaigns for the general public using different media. For improved screening strategies and public awareness, novel approaches have to be developed and evaluated. Finally, guidelines should be actively disseminated to all medical practitioners to increase their use in daily practice. Although the major socioeconomic and public health concerns of C. trachomatis infection are recognized, several considerations and additional measures for addressing this increasingly urgent health problem remain.

Screening for bacterial vaginosis at the time of intrauterine contraceptive device insertion: is there a role?
Pham AT, Kives S, Merovitz L, Nitsch R, Tessler K, Yudin MH
J Obstet Gynaecol Can. 2012 Feb;34(2):179-85.

OBJECTIVE: To estimate the prevalence of bacterial vaginosis (BV) among women attending outpatient gynaecology clinics for insertion of an intrauterine contraceptive device (IUD); and to describe any differences between BV-positive and BV-negative women at one month after insertion with respect to four primary clinical outcomes: expulsion of IUD, pain, fever > 38ºC, and heavy bleeding. METHODS: We carried out an observational prevalence study between March 2008 and March 2009. Seventy women were each followed for one month. Vaginal cultures for BV were obtained before and at one month after IUD insertion, and women were assessed for complications at one month after insertion. Thirty-eight women had a copper IUD (Cu-IUD) inserted and 32 had a levonorgestrel-releasing IUD (LNG-IUD) inserted. Bacterial vaginosis was diagnosed using Nugent's scoring and Gram stain evaluation of the cultures. Frequency distributions, Student t test, and Fisher exact test of independence were used to analyze the data. RESULTS: The prevalence of BV was 7.1%. Five women were found to be BV positive at the time of IUD insertion, and none experienced any clinical complications. One BV-negative patient developed a tubo-ovarian abscess three months after

LNG-IUD insertion, and another BV-negative patient reported persistent, thick vaginal discharge after Cu-IUD insertion. Of 43 BV-negative patients who had repeat cultures performed at their one-month follow-up visit, four (9.3%) shifted from having normal flora to being BV positive. We found no significant relationship between a patient's BV status and any clinical outcome. CONCLUSION: The incidence of BV in this study was lower than that described in other populations. No clinical complications occurred among the BV-positive women. Screening for BV prior to IUD insertion is neither currently recommended, nor supported by our study findings.

Treatment of postmenopausal vaginal atrophy with 10-µg estradiol vaginal tablets.
Panay N, Maamari R
Menopause Int. 2012 Mar;18(1):15-9.

Postmenopausal estrogen deficiency can lead to symptoms of urogenital atrophy. Individuals with urogenital atrophy have symptoms that include vaginal dryness, vaginal and vulval irritation, vaginal soreness, pain and burning during urination (dysuria), increased vaginal discharge, vaginal odour, vaginal infections, recurrent urinary tract infections, pain associated with sexual activity (dyspareunia) and vaginal bleeding associated with sexual activity. Despite the frequency and effects of vaginal atrophy symptoms, they are often under-reported and, consequently, under-treated. Therefore, care of a menopausal woman should include a physical assessment of vaginal atrophy and a dialogue between the physician and the patient that explores existing symptoms and their effect on vulvovaginal health, sexuality and quality-of-life issues. The development of the ultra-low-dose 10-µg estradiol vaginal tablets is in line with the requirements of regulatory agencies and women's health societies regarding the use of the lowest effective hormonal dose. Because of its effectiveness and safety profiles, in addition to its minimal systemic absorption, the 10-µg estradiol vaginal tablet can offer greater reassurance to health-care providers and postmenopausal women with an annual estradiol administration of only 1.14 mg.

Genital and inguinal cutaneous toxicity in male and female patients treated with sunitinib.
Iacovelli R, Mancini ML, Risi E, Palazzo A, Cortesi E
Int J Dermatol. 2012 Feb;51(2):221-2. doi: 10.1111/j.1365-4632.2011.05057.x.

BACKGROUND: Sunitinib is an orally tyrosine kinase inhibitor currently approved by the Food and Drug Administration for the treatment of advanced renal cell carcinoma (RCC) and gastrointestinal stromal tumor. Several cutaneous toxicities have been observed with Sunitinib and among those scrotal cutaneous toxicity could affect 12.5% of patients after an average 66 days of exposure to treatment. OBJECTIVE: We report the first case of a female patient who develops vulvar toxicity during sunitinib treatment. Subjects and METHODS: A 68-year-old female patient was treated with sunitinib at standard dose of 50 mg/daily for four weeks on and two weeks off, for advanced clear cell RCC. During week 2 of the second cycle of sunitinib, the patient reported vulvar pain and itching. RESULTS: Local examination revealed erythema of the outer lips and two erythematosus areas localized on the upper medial area of the legs. The sunitinib was discontinued, and the signs and symptoms disappeared completely seven days after drug interruption without any specific treatment. CONCLUSION: Female genital cutaneous toxicity with sunitinib shows a similar behavior as found in males, and both should be carefully evaluated even if the treatment discontinuation is generally not required.

Untangling a web: An unusual case of labial necrosis in an adolescent female.
Stock C, Wang LC, Spigland NA
J Pediatr Adolesc Gynecol. 2011 Dec 27. [Epub ahead of print]

BACKGROUND: Hair tourniquets are commonly described in the pediatric literature. Prompt recognition of a hair tourniquet and treatment with complete removal of the hair by pediatricians, pediatric emergency room physicians, or gynecologists is essential to prevent ischemia and necrosis of affected tissue. CASE: Herein we present the case of a 12-

year-old female referred to the pediatric surgery clinic for labial pain and swelling. She was found to have a hair tourniquet of the labia minora caused by pubic hair. The patient was taken to the operating room for examination under anesthesia and removal of the hair. Her post-operative course was unremarkable and she was discharged home the following day. On follow-up visit to the clinic her labial edema had completely resolved and she was pain free. SUMMARY AND CONCLUSIONS: Unlike previous case reports that describe hair tourniquets as originating from hair on the head, our patient had a hair tourniquet caused by pubic hair. In adolescents where personal hygiene of the perineum is difficult, clinicians need to be aware of the possibility of a hair tourniquet forming from pubic hair.

The effect of prolapse repair on sexual function in women.
Dua A, Jha S, Farkas A, Radley S
J Sex Med. 2012 Feb 29. doi: 10.1111/j.1743-6109.2012.02660.x. [Epub ahead of print]

INTRODUCTION: Sexual dysfunction is common in women with pelvic organ prolapse (POP). Treatment of symptomatic prolapse often requires surgery. The outcome of prolapse symptoms following surgery is well studied and reported, but evidence on outcomes of sexual function following pelvic reconstructive surgeries is limited. AIM: The objective of this study was to assess the impact of different forms of surgery for POP on sexual function using prospectively collected data. METHODS: In this ethically approved project, data were collected prospectively for women undergoing prolapse repair between 2008 and 2010 and were stratified into four groups: "posterior repair," "anterior repair," "anterior repair with vaginal hysterectomy," and "combined anterior and posterior repair." The electronic personal assessment questionnaire-pelvic floor (ePAQ-PF) was used to assess symptoms. The sexual dimension of ePAQ-PF computes domain scores for sexual dysfunction secondary to vaginal symptoms and dyspareunia on a scale of 0-100 (0=best possible and 100=worst possible health status). ePAQ-PF was completed in 123 sexually active women both pre- and 3-6 month postoperatively. Results were analyzed using SPSS (SPSS Inc., Chicago, IL, USA). Pre- and postoperative scores for each domain were compared in all groups (Student's t-test). Individual symptoms in these domains were compared using Wilcoxon signed-rank test. MAIN OUTCOME MEASURES: Change in sexual symptoms and dyspareunia following prolapse surgery in each group. RESULTS: Women undergoing anterior repair or anterior repair and vaginal hysterectomy reported significant improvement in sexual symptoms and dyspareunia. Women undergoing a posterior repair in isolation had improved sexual function following surgery though improvement in dyspareunia was not significant. Women undergoing combined anterior and posterior repair had the least improvement in sexual function. CONCLUSIONS: Sexual function improves in women following pelvic reconstructive surgery, but the improvement is more substantial following anterior repair either alone or in combination with a vaginal hysterectomy when compared with posterior repair.

Acute genital ulcers in nonsexually active young girls: Case series, review of the literature, and evaluation and management recommendations.
Rosman IS, Berk DR, Bayliss SJ, White AJ, Merritt DF
Pediatr Dermatol. 2012 Feb 3. doi: 10.1111/j.1525-1470.2011.01589.x. [Epub ahead of print]

Acute genital ulcers rarely occur in nonsexually active young girls. When present, they can cause significant physical and emotional distress for the patient and her parents, and prompt an evaluation for sexual abuse and sexually transmitted diseases. With this review, we aim to further characterize acute genital ulcers in nonsexually active young girls by reviewing the medical records of patients with this disorder and to offer an approach to the diagnosis, evaluation, and treatment of acute genital ulcers based on our understanding and knowledge of this condition. We retrospectively review our understanding and knowledge of acute genital ulcers in nonsexually active girls at a pediatric hospital. A review of the recent literature on acute genital ulcers and a multidisciplinary approach to the diagnosis, evaluation, and treatment of acute genital ulcers are also presented. Twelve patients presented with acute genital ulcers, 11 of which were hospitalized for evaluation and pain management. Extensive work-up failed to reveal a specific infectious or autoimmune etiology in all but one patient, who was diagnosed with acute mycoplasma pneumonia. Acute genital ulcers in nonsexually active young girls likely represent a form of idiopathic vulvar aphthosis. Evaluation of a first episode of

acute genital ulcers with mild prodromal symptoms should be limited. Treatment consists primarily of supportive care and symptom relief.