

## **NVA Research Update E-Newsletter**

July 2013

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This e-newsletter, which contains abstracts of recently published articles relevant to the study and medical management of vulvodynia, has been supported, in part, through a grant from the **Enterprise Holdings Foundation**.

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### **Vulvodynia /Vulvovaginal Pain**

#### **Perceived stereotyping and seeking care for chronic vulvar pain.**

Nguyen RH, Turner RM, Rydell SA, Maclehose RF, Harlow BL  
Pain Med. 2013 Jun 6. doi: 10.1111/pme.12151. [Epub ahead of print]

**OBJECTIVES:** We examined stereotyping of chronic pain sufferers among women aged 18-40 years and determined whether perceived stereotyping affects seeking care for women with chronic vulvar pain. **DESIGN:** Cross-sectional study using a community-based survey of vulvodynia asking if "Doctors think that people with chronic pain exaggerate their pain," and if "People believe that vulvar pain is used as an excuse to avoid having sex". **SETTING AND PARTICIPANTS:** Twelve thousand eight hundred thirty-four women aged 18-40 years in metropolitan Minneapolis/St. Paul, Minnesota. **OUTCOME MEASURES:** Women were considered to have a history of chronic vulvar pain if they reported vulvar burning lasting more than 3 months or vulvar pain on contact. **RESULTS:** Four thousand nine hundred eighty-seven (38.9%) women reported a chronic pain condition; 1,651 had chronic vulvar pain. Women experiencing chronic pain were more likely than those without to perceive stereotyping from both doctors and others; a dose-response with the number of pain conditions existed. Women with chronic vulvar pain were more likely to believe that people think vulvar pain is an excuse to avoid intercourse. Half of the women with chronic vulvar pain did not seek medical care for it; of these, 40.4% perceived stereotyping from doctors. However, it was women who actually sought care (45.1%) who were more likely to feel stigmatized by doctors (adjusted relative risk = 1.11, 95% confidence interval: 1.01-1.23). **CONCLUSIONS:** Perceived negative stereotyping among chronic pain sufferers is common, particularly negative perceptions about physicians. In fact, chronic vulvar pain sufferers who felt stigmatized were more likely to have sought care than those who did not feel stigmatized.

#### **Rationale and design of a multicenter randomized clinical trial of extended release gabapentin in provoked vestibulodynia and biological correlates of response.**

Brown CS, Foster DC, Wan JY, Rawlinson L, Bachmann GA  
Contemp Clin Trials. 2013 Jun 29. doi: 10.1016/j.cct.2013.06.015. [Epub ahead of print]

**INTRODUCTION:** Few randomized controlled trials (RCTs) have been conducted to establish evidence-based management protocols for provoked vestibulodynia (PVD), a chronic vulvar pain condition affecting approximately 14 million women in the U.S. We describe the rationale and design of an NIH funded multicenter clinical trial utilizing an extended release formulation of gabapentin (G-ER), an intervention that preliminary data suggest may be efficacious for this condition. **OBJECTIVES:** 1) to determine if pain from tampon insertion (primary outcome measure) is lower in PVD patients when treated with G-ER compared to when treated with placebo and 2) to determine if G-ER reduces vulvar mechanical hyperalgesia, vaginal muscle pain to palpation, the number and intensity of somatic tender points, spontaneous and provoked pain to intradermal capsaicin with an accompanying increase in cardiac beat-to-beat variability and to identify mechanistically-based PVD subtypes. Additional outcomes include subject reported intercourse pain and summative 24-hour pain. **METHODS:** This 16-week, randomized, double-blind, placebo-controlled, crossover study will enroll 120 women 18 years and older who report tenderness localized to the vulvar vestibule, pain

with tampon insertion, and, when sexually active, insertional dyspareunia. Electronically entered daily diaries will be used to determine if pain is lower in PVD subjects when treated with G-ER (up to 3000mg/d) compared to when treated with placebo. Psychophysiological measures will be obtained at baseline and after 2 weeks at the maximum tolerated dose. CONCLUSION: We will conduct the first multicenter RCT to confirm efficacy of an agent that is currently used in clinical practice for treating PVD.

### **The treatment of vestibulodynia with topical estradiol and testosterone.**

Burrows LJ, Goldstein AT

Sex Med. 16 Jul 2013. doi: 10.1002/sm2.4

INTRODUCTION: Combined hormonal contraceptives (CHCs) use is becoming an increasingly recognized cause of vestibulodynia. AIM: This study aims to describe pre- and post-treatment vestibular pain, sex hormone binding globulin (SHBG), and calculated free testosterone levels in women undergoing treatment for vestibulodynia. METHODS: This was a chart review of 50 premenopausal women who presented with vestibular pain while currently using CHCs. Pre- and post-treatment vestibular pain, SHBG, and calculated free testosterone levels were assessed. RESULTS: There was a statistically significant improvement in post-treatment vestibular pain scores ( $P = 0.001$ ), SHBG ( $P = 0.001$ ), and calculated free testosterone ( $P = 0.001$ ) levels from baseline. CONCLUSION: Women with vestibulodynia that began while on CHC may effectively be treated by discontinuing the CHC combined with the application topical hormone therapy. Symptomatic improvement is accompanied by normalization of calculated free testosterone and SHBG values.

### **Secondary provoked vestibulodynia in sexually active women with uncomplicated recurrent urinary tract infections.**

Salonia A, Clementi MC, Graziottin A, Nappi RE, Castiglione F, Ferrari M, Capitanio U, Damiano R, Montorsi F

J Sex Med. 2013 Jul 22. doi: 10.1111/jsm.12242. [Epub ahead of print]

INTRODUCTION: Uncomplicated recurrent urinary tract infections (rUTIs) associated with uropathogenic *Escherichia coli* (UPEC) are common among healthy, reproductive-aged women. Provoked vestibulodynia (PVD) is a major reason of sexual pain in premenopausal women. AIM: The aim of this paper is to assess prevalence and predictors of secondary PVD in a cohort of Caucasian-European, heterosexual, sexually active, reproductive-aged women seeking medical help for rUTIs as their primary complaint. METHODS: Clinical and psychometric variables for 60 consecutive patients with rUTIs were considered. Patients were assessed with a thorough medical and sexual history, a number of psychometric instruments, and a specific physical examination. Urinalysis and self-collected urine cultures from the previous 12 months were also examined. MAIN OUTCOME MEASURE: Descriptive statistics and logistic regression models were used to test the associations between secondary PVD and sociodemographic and clinical variables. RESULTS: Mean age was 34.2 years (median 33 years; range 21-42). Secondary PVD was found in 36 of 60 patients (60%). Women with PVD had a higher prevalence of urinary tract infections (UTIs) over the previous 12 months ( $\chi^2 : 4.54$ ;  $P = 0.03$ ) and suffered more frequently from UPEC-related rUTIs ( $\chi^2 : 5.92$ ;  $P = 0.01$ ) than those without PVD. Moreover, women with PVD showed significantly lower scores on Female Sexual Function Index domains (all  $P \leq 0.01$ ), as compared with PVD-negative women. UPEC-related rUTIs (odds ratio [OR]: 3.1;  $P = 0.01$ ), six or more UTIs over the previous 12 months (OR: 2.8;  $P = 0.01$ ), and treatment with three or more antibiotics throughout the same period (OR: 2.1;  $P = 0.04$ ) emerged as independent predictors of PVD. CONCLUSIONS: Three of five Caucasian-European, heterosexual, sexually active women of reproductive age complaining of rUTIs as their primary disorder also suffer from secondary PVD. Uncomplicated UPEC-related rUTIs are more frequently associated with secondary PVD than are UTIs caused by different uropathogens.

### **Central sensitization in urogynecological chronic pelvic pain: a systematic literature review.**

Kaya S, Hermans L, Willems T, Roussel N, Meeus M

Pain Phys. Jul 2013;16;291-308.

BACKGROUND: Chronic pelvic pain (CPP) is a complex pain syndrome. Since its pathogenesis is still poorly understood and structural alterations in pain related brain regions may be present, there is a greater acceptance that sensitization of the central nervous system (CNS) plays an important role in the development and maintenance of chronicity. OBJECTIVE:

The purpose of this study is to systematically review the scientific evidence regarding central sensitization (CS) in female patients with urogynecological CPP. **STUDY DESIGN:** Systematic review of the literature. **METHODS:** A systematic literature search was conducted in PubMed and Web of Science using different keyword combinations related to urogynecological CPP and central sensitization. Full text clinical reports addressing CS in adult women with urogynecological CPP were included and assessed for methodological quality by 2 independent reviewers. **RESULTS:** After screening for the eligibility, a total of 29 full-text articles with low to good methodological quality were retained. All studies were observational, 27 of which were case-control and 2 of which were cohorts. Sensitivity of the CNS was investigated by using a variety of methods. Although different central mechanisms seem to be involved in pain processing, the present evidence suggests hyperexcitability of the CNS in patients with urogynecological CPP. Altered brain morphology and function, generalized hyperalgesia to different type of stimuli, overactive bottom-up nociceptive mechanisms, and autonomic dysregulation were established in patients with urogynecological CPP. Nevertheless, diffuse noxious inhibitory control seemed normal, and therefore the contribution of an impaired endogenous pain inhibition mechanism to CPP requires further study. The same goes for the contribution of psychological factors. **LIMITATIONS:** The level of evidence of retained studies is low due to the observational study designs and a wide range of diagnoses and assessment methods. **CONCLUSION:** Although the majority of the literature provides evidence for the presence of CS in urogynecological CPP with changes in brain morphology/function and sensory function, it is unclear whether these changes in central pain processing are secondary or primary to CPP, especially since evidence regarding the function of endogenous pain inhibition and the role of psychosocial pain facilitation is scarce. Further studies with good methodological quality are needed in order to clarify exact mechanisms.

**Sexual and relationship intimacy among women with provoked vestibulodynia and their partners: associations with sexual satisfaction, sexual function, and pain self-efficacy.**

Bois K, Bergeron S, Rosen NO, McDuff P, Grégoire C

J Sex Med. 2013 Jun 26. doi: 10.1111/jsm.12210. [Epub ahead of print]

**INTRODUCTION:** Provoked vestibulodynia (PVD) is the most frequent subtype of vulvodynia. Women report negative consequences of PVD on their sexual and romantic relationships. Researchers have recently highlighted the importance of examining interpersonal factors such as intimacy, and of including both women and their partners in study designs. **AIM:** The aim of this study was to investigate sexual and relationship intimacy as defined by the Interpersonal Process Model of Intimacy and their associations with sexual satisfaction, sexual function, pain self-efficacy, and pain intensity among women with PVD and their partners. **METHODS:** Ninety-one heterosexual women (M age = 27.38, SD = 6.04) diagnosed with PVD and their partners (M age = 29.37, SD = 7.79) completed measures of sexual and relationship intimacy, sexual satisfaction, sexual function, pain self-efficacy, and pain intensity. **MAIN OUTCOME MEASURES:** Dependent measures were the (i) Global Measure of Sexual Satisfaction Scale; (ii) Female Sexual Function Index; (iii) Painful Intercourse Self-Efficacy Scale; and (iv) visual analog scale of pain intensity during intercourse. **RESULTS:** After controlling for women's age, women's greater sexual intimacy ( $\beta = 0.49$ ,  $P < 0.001$ ) was associated with women's greater sexual satisfaction and higher pain self-efficacy ( $\beta = 0.39$ ,  $P = 0.001$ ), beyond the effects of partners' sexual intimacy. Also, women's greater sexual intimacy ( $\beta = 0.24$ ,  $P = 0.05$ ) and women's greater relationship intimacy ( $\beta = 0.54$ ,  $P = 0.003$ ) were associated with greater women's sexual function, beyond the effects of partners' sexual and relationship intimacy. **CONCLUSIONS:** Women's self-reported sexual and relationship intimacy in the couple relationship may promote higher sexual satisfaction, sexual function, and pain self-efficacy, as well as possibly foster greater sexual well-being among women with PVD. The authors discuss implications for the inclusion of emotional and interpersonal aspects of the couple's dynamic in clinical interventions and future research in PVD.

**Sexual and relationship satisfaction and vestibular pain sensitivity among women with provoked vestibulodynia.**

Smith KB, Pukall CF, Chamberlain SM

J Sex Med. 2013 Jun 19. doi: 10.1111/jsm.12213. [Epub ahead of print]

**INTRODUCTION:** Provoked vestibulodynia (PVD) is a common cause of painful intercourse. Despite the fact that PVD is associated with high levels of pain and negative impact on women's sexuality, research has not examined associations between affected women's pain sensitivity and their sexual and relationship satisfaction. **AIMS:** This study aimed to

examine sexual and relationship functioning/satisfaction and vestibular pain sensitivity among PVD-affected women, and potential associations between these variables. **METHODS:** Participants were 17 women with PVD and 17 matched controls. Women were assessed via a gynecological examination, structured interview, and the Female Sexual Function Index (FSFI), Golombok Rust Inventory of Sexual Satisfaction (GRISS), and Dyadic Adjustment Scale (DAS). Additionally, women completed a quantitative sensory testing session to assess vestibular pain thresholds and associated pain ratings; specifically, vestibular pressure-pain and heat pain thresholds were measured. **MAIN OUTCOME MEASURES:** Gynecological and intercourse pain ratings; FSFI; GRISS; DAS; vestibular pressure-pain threshold; and vestibular heat pain thresholds. **RESULTS:** PVD-affected women reported significantly decreased sexual function in comparison with controls. While no differences in relationship satisfaction were found between groups, women with PVD did report less sexual satisfaction on the FSFI. PVD-affected women also reported significantly higher vestibular pain ratings associated with the gynecological examination and heat pain tolerance procedures, and lower pressure-pain threshold, heat pain threshold, and heat pain tolerance at the vestibule in comparison with controls. Among women with PVD, lower heat pain threshold was associated with less sexual satisfaction, and higher pain ratings related to intercourse and heat pain tolerance, respectively, were associated with lower sexual function and satisfaction. **CONCLUSIONS:** The results indicate that women with PVD experience negative sexual effects and increased pain sensitivity. This study also suggests that some aspects of pain may be related to lower levels of sexual function and satisfaction among affected women.

### **Sexual behaviors in women with primary and secondary provoked vestibulodynia: A controlled study.**

Lambert B, Desrosiers M, Chagnon M, Lepage Y

Adv. Sex. Med. July 2013. doi: 10.4236/asm.2013.33010

**INTRODUCTION:** Provoked vestibulodynia affects 12% of the general female population and more specifically, 21% of women aged less than 30 years. Primary and secondary vestibulodynia are hypothesized to represent the endpoints of different etiologic pathways, although there is still little research addressing potential distinctions between these two groups, particularly with regard to sexuality. **AIMS:** To compare sexual activity and behavior of women with provoked primary vestibulodynia (PVD1) and secondary vestibulodynia (PVD2) against age-matched controls. **METHODS:** Fifty-seven participants (N = 57), mean age 25.72 (18 - 41) recruited from a gynecology clinic underwent a gynaecological examination and completed a self-report questionnaire: 20 (N = 20) were diagnosed with primary provoked vestibulodynia (PVD1), 19 (N = 19) with secondary provoked vestibulodynia (PVD2), and 18 (N = 18) were medically confirmed as no-pain controls. **MAIN OUTCOME:** To verify any differences in the sexual behavior between primary, secondary vestibulodynias and controls. **RESULTS:** Mean pain duration differed significantly in participants with PVD1 at 73.8 months against those with PVD2 at 37.4 months ( $p = 0.003$ ). Frequency of sexual activity also differed significantly between the three groups ( $p = 0.012$ ): the controls were at 27.8% against 0% in primary and secondary vestibulodynias for once or more a day. No significant difference was observed for the sexual arousal time and masturbation frequency. Vaginal penetration was overrepresented in controls ( $p < 0.001$ ) contrary to fellatio frequency ( $p = 0.016$ ). Pain digital test was significantly different between the three groups in one finger (3.85 vs. 0.08), two fingers (4.39 vs. 0.06) or three fingers (5.39 vs. 0.56) (PVD1 against controls), lubricated inserted fingers for pain verification ( $p < 0.001$ ). **CONCLUSIONS:** Provoked vestibulodynia generates problems in the sexual response and coital activity, notably in the masturbatory activity and oral receptive female sex.

### **A comparative study of sexual function, behavior, and cognitions of women with lifelong vaginismus.**

Cherner RA, Reissing ED

Arch Sex Behav. 2013 Jun 4. [Epub ahead of print]

Vaginismus is classified as a sexual dysfunction, yet limited research is available on the sexual function and behavior of women with this condition. Comparing women with lifelong vaginismus to women with lifelong dyspareunia and women with no pain during intercourse, this study explored sexual function, anxiety, and behavior along with cognitions related to vaginal penetration. A total of 152 women completed an online survey that included a series of validated questionnaires. Main findings indicated that, relative to both comparison groups, women in the vaginismus group reported a more limited range of sexual behavior across the lifespan and more maladaptive cognitions related to fear of losing control of one's body and the situation during penetration. Compared to the no-pain group, both symptomatic

groups reported more difficulties across several indicators of sexual function, more limited sexual behavior in the past year and past month, and more maladaptive cognitions related to vaginal penetration. However, women with vaginismus reported more sexual desire and less difficulty with lubrication compared to women with dyspareunia. Numerous sexual problems extending beyond vaginal penetration difficulties were confirmed, suggesting a need for broader treatment approaches not limited to the experience of vaginal penetration. Results were discussed as they relate to the fear-avoidance model of vaginismus.

### **Aspects of sexual self-schema in premenopausal women with dyspareunia: associations with pain, sexual function, and sexual distress.**

Pazmany E, Bergeron S, Van Oudenhove L, Verhaeghe J, Enzlin P  
J Sex Med. 2013 Jul 11. doi: 10.1111/jsm.12237.

**INTRODUCTION:** Although it is known that women with dyspareunia suffer from impaired psychological and sexual functioning, the study of the various dimensions of sexual self-schema and their associations with these outcomes has been neglected. **AIM:** To examine whether self-image cognitions about vaginal penetration, body image, and feelings and beliefs about one's own genitals contribute to the variance in pain, sexual functioning, and sexual distress. **METHODS:** Premenopausal women (n = 231; M age = 24.85, SD = 5.55) with self-reported dyspareunia completed an online survey focusing on self-image cognitions about vaginal penetration, body image, female genital self-image, pain during intercourse, sexual functioning, sexual distress, anxiety, and catastrophizing. **MAIN OUTCOME MEASURES:** (i) Pain intensity during intercourse, (ii) the Female Sexual Function Index without the Pain subscale, and (iii) the Female Sexual Distress Scale. **RESULTS:** Controlling for anxiety and catastrophizing, negative self-image cognitions about vaginal penetration, negative body image, and negative genital self-image together accounted for a portion of the variance in increased pain intensity, sexual dysfunction, and sexual distress. However, only self-image cognitions about vaginal penetration ( $\beta = 0.25$ ,  $P = 0.005$ ) contributed uniquely to the variance in pain intensity, whereas self-image cognitions about vaginal penetration ( $\beta = -0.18$ ,  $P = 0.048$ ) and genital self-image ( $\beta = 0.21$ ,  $P = 0.008$ ) contributed independently to the variance in sexual functioning. Finally, self-image cognitions about vaginal penetration ( $\beta = 0.28$ ,  $P < 0.001$ ), body image ( $\beta = 0.24$ ,  $P < 0.001$ ) and genital self-image ( $\beta = -0.14$ ,  $P = 0.006$ ) each contributed independently to the variance in sexual distress. **CONCLUSIONS:** Findings suggest that self-image cognitions about vaginal penetration and feelings and beliefs about one's own body and genitals are associated with pain and sexuality outcomes in women with dyspareunia.

## **Chronic Pain**

### **The development of chronic pain: physiological CHANGE necessitates a multidisciplinary approach to treatment.**

Pergolizzi J, Ahlbeck K, Aldington D, Alon E, Coluzzi F, Dahan A, Huygen F, Kocot-Kępska M, Mangas AC, Mavrocordatos P, Morlion B, Müller-Schwefe G, Nicolaou A, Pérez Hernández C, Sichère P, Schäfer M, Varrassi G  
Curr Med Res Opin. 2013 Jul 3. [Epub ahead of print]

Chronic pain is currently under-diagnosed and under-treated, partly because doctors' training in pain management is often inadequate. This situation looks certain to become worse with the rapidly increasing elderly population unless there is a wider adoption of best pain management practice. This paper reviews current knowledge of the development of chronic pain and the multidisciplinary team approach to pain therapy. The individual topics covered include nociceptive and neuropathic pain, peripheral sensitization, central sensitization, the definition and diagnosis of chronic pain, the biopsychosocial model of pain and the multidisciplinary approach to pain management. This last section includes an example of the implementation of a multidisciplinary approach in Belgium and describes the various benefits it offers; for example, the early multidimensional diagnosis of chronic pain and rapid initiation of evidence-based therapy based on an individual treatment plan. The patient also receives continuity of care, while pain relief is accompanied by improvements in physical functioning, quality of life and emotional stress. Other benefits include decreases in catastrophizing, self-reported patient disability, and depression. Improved training in pain management is clearly needed, starting with the undergraduate medical curriculum, and this review is intended to encourage further study by those who manage patients with chronic pain.

### **Skin matters: identifying pain mechanisms and predicting treatment outcomes.**

Shipton EA

Neurol Res Int. 2013;2013:329364. doi: 10.1155/2013/329364.

The skin acts as a complex sensory organ. The emerging new data on peripheral pain mechanisms from within the skin is presented. This data has led to new insights into the potential pain mechanisms for various pain conditions including neuropathic pain (from small fiber neuropathies) and Complex Regional Pain Syndrome. The somatosensory neurons that innervate our skin constantly update our brains on the objects and environmental factors that surround us. Cutaneous sensory neurons expressing nociceptive receptors such as transient receptor potential vanilloid 1 channels and voltage-gated sodium channels are critical for pain transmission. Epidermal cells (such as keratinocytes, Langerhans cells, and Merkel cells) express sensor proteins and neuropeptides; these regulate the neuroimmunocutaneous system and participate in nociception and neurogenic inflammation. In the past two decades, there has been widespread use of modalities such as punch skin biopsies, quantitative sensory testing, and laser-evoked potentials to evaluate small caliber nerve fibers. This paper explores these laboratory techniques as well as the phenomenon of small fiber neuropathy. Treatment using transdermal drug delivery is discussed. There is potential for these findings to predict treatment outcomes in clinical practice and to develop new therapies for different pain conditions. These findings should enhance the physician's ability to evaluate and treat diverse types of pain.

### **Neuropathic pain and pharmacological treatment.**

Jongen JL, Hans G, Benzon HT, Huygen F, Hartrick CT

Pain Pract. 2013 Jun 10. doi: 10.1111/papr.12085. [Epub ahead of print]

Neuropathic pain is a serious chronic condition strongly affecting quality of life, which can be relieved but cannot be cured. Apart from symptomatic management, treatment should focus on the underlying disorder. The estimated prevalence is at least 1% to 5% of the general population. Neuropathic pain is characterized both by spontaneous and evoked pain. A diagnosis of neuropathic pain can usually be established based solely on history and neurological examination. Ancillary investigations may include EMG and computerized tomography/magnetic resonance imaging scans, depending on the localization of the suspected lesion. A limited number of agents, primarily directed at symptom control, are currently approved for use in neuropathic pain. A mechanism-based approach to pharmacological intervention supports the use of polypharmacy in neuropathic pain.

### **The neurology of itch.**

Dhand A, Aminoff MJ

Brain. 2013 Jun 22. [Epub ahead of print]

Research over the past 15 years has helped to clarify the anatomy and physiology of itch, the clinical features of neuropathic itch syndromes and the scientific underpinning of effective treatments. Two itch-sensitive pathways exist: a histamine-stimulated pathway that uses mechanically insensitive C-fibers, and a cowhage-stimulated pathway primarily involving polymodal C-fibers. Interactions with pain continue to be central to explaining various aspects of itch. Certain spinal interneurons (Bhlhb5) inhibit itch pathways within the dorsal horn; they may represent mediators between noxious and pruritic pathways, and allow scratch to inhibit itch. In the brain, functional imaging studies reveal diffuse activation maps for itch that overlap, but not identically, with pain maps. Neuropathic itch syndromes are chronic itch states due to dysfunction of peripheral or central nervous system structures. The most recognized are postherpetic itch, brachioradial pruritus, trigeminal trophic syndrome, and ischaemic stroke-related itch. These disorders affect a patient's quality of life to a similar extent as neuropathic pain. Treatment of neuropathic itch focuses on behavioral interventions (e.g., skin protection) followed by stepwise trials of topical agents (e.g., capsaicin), antiepileptic drugs (e.g., gabapentin), injection of other agents (e.g., botulinum A toxin), and neurostimulation techniques (e.g., cutaneous field stimulation). The involved mechanisms of action include desensitization of nerve fibers (in the case of capsaicin) and postsynaptic

blockade of calcium channels (for gabapentin). In the future, particular histamine receptors, protease pathway molecules, and vanilloids may serve as targets for novel antipruritic agents.

### **Platelet-rich plasma and the elimination of neuropathic pain.**

Kuffler DP

Mol Neurobiol. 2013 Jul 7. [Epub ahead of print]

Peripheral neuropathic pain typically results from trauma-induced nociceptive neuron hyperexcitability and their spontaneous ectopic activity. This pain persists until the trauma-induced cascade of events runs its full course, which results in complete tissue repair, including the nociceptive neurons recovering their normal biophysical properties, ceasing to be hyperexcitable, and stopping having spontaneous electrical activity. However, if a wound undergoes no, insufficient, or too much inflammation, or if a wound becomes stuck in an inflammatory state, chronic neuropathic pain persists. Although various drugs and techniques provide temporary relief from chronic neuropathic pain, many have serious side effects, are not effective, none promotes the completion of the wound healing process, and none provides permanent pain relief. This paper examines the hypothesis that chronic neuropathic pain can be permanently eliminated by applying platelet-rich plasma to the site at which the pain originates, thereby triggering the complete cascade of events involved in normal wound repair. Many published papers claim that the clinical application of platelet-rich plasma to painful sites, such as muscle injuries and joints, or to the ends of nerves evoking chronic neuropathic pain, a process often referred to as prolotherapy, eliminates pain initiated at such sites. However, there is no published explanation of a possible mechanism/s by which platelet-rich plasma may accomplish this effect. This paper discusses the normal physiological cascade of trauma-induced events that lead to chronic neuropathic pain and its eventual elimination, techniques being studied to reduce or eliminate neuropathic pain, and how the application of platelet-rich plasma may lead to the permanent elimination of neuropathic pain. It concludes that platelet-rich plasma eliminates neuropathic pain primarily by platelet- and stem cell-released factors initiating the complex cascade of wound healing events, starting with the induction of enhanced inflammation and its complete resolution, followed by all the subsequent steps of tissue remodeling, wound repair and axon regeneration that result in the elimination of neuropathic pain, and also by some of these same factors acting directly on neurons to promote axon regeneration thereby eliminating neuropathic pain.

### **Prevalence, causes, severity, impact, and management of chronic pain in Australian general practice patients.**

Henderson JV, Harrison CM, Britt HC, Bayram CF, Miller GC

Pain Med. 2013 Jul 15. doi: 10.1111/pme.12195

**OBJECTIVE:** To determine the prevalence of chronic pain, its causes, severity, management, impact on sleep, mood and activity levels, and general practitioner (GP) and patient satisfaction with pain management. **DESIGN:** A subset of 197 GPs and 5,793 patients from the BEACH program, a continuous, national cross-sectional survey of Australian general practice. **RESULTS:** The prevalence of chronic pain was 19.2% (95% confidence interval: 17.4–21.0) (N = 1,113). The most commonly reported causal conditions were osteoarthritis (48.1%) and back problems (29.4%). For pain severity (using Von Korff's pain grades), 25.2% were at Grade I (lowest); 37.1% were at Grade II; 28.3% at Grade III; and 9.4% at Grade IV (highest). Medication was used for pain management by 86.1% of patients, and one third also used nonpharmacological managements. One third of patients were taking opioids, most commonly those at the highest pain severity grades. On "Live Better with Pain Log" scale, the impact of pain was similar across activity (mean = 4.0), sleep (mean = 4.8), and mood (mean = 4.8). On a scale of 1 (highest) to 5 (lowest), GPs' satisfaction (mean = 2.5) was highly correlated ( $r = 0.7$ ) with patients' satisfaction (mean = 2.6) with pain management. **CONCLUSIONS:** Chronic pain impairs patient quality of life, and is a public health burden. This study provides a national overview of the prevalence, causes, severity, management and impact of chronic pain in Australian general practice patients, and the parity between GP and patient satisfaction with pain management.

### **The relation between pain-related fear and disability: a meta-analysis.**

Zale EL, Lange KL, Fields SA, Ditte JW

J Pain. 2013 Jul 11. doi: 10.1016/j.jpain.2013.05.005

Within a biopsychosocial framework, psychological factors are thought to play an important role in the onset and progression of chronic pain. The cognitive-behavioral fear-avoidance model of chronic pain suggests that pain-related fear contributes to the development and maintenance of pain-related disability. However, investigations of the relation between pain-related fear and disability have demonstrated considerable between-study variation. The main goal of the current meta-analysis was to synthesize findings of studies investigating cross-sectional associations between pain-related fear and disability in order to estimate the magnitude of this relation. We also tested potential moderators, including type of measure used, demographic characteristics, and relevant pain characteristics. Searches in PubMed and PsycINFO yielded a total of 46 independent samples (N = 9,579) that reported correlations between pain-related fear and disability among persons experiencing acute or chronic pain. Effect size estimates were generated using a random-effects model and artifact distribution method. The positive relation between pain-related fear and disability was observed to be moderate to large in magnitude, and stable across demographic and pain characteristics. Although some variability was observed across pain-related fear measures, results were largely consistent with the fear-avoidance model of chronic pain.

### **Attributes associated with patient perceived outcome in an academic chronic pain clinic.**

Trentman TL, Chang YH, Chien JJ, Rosenfeld DM, Gorlin AW, Seamans DP, Freeman JA, Wilshusen LL

Pain Pract. 2013 May 22. doi: 10.1111/papr.12077. [Epub ahead of print]

**OBJECTIVES:** Patient satisfaction is tied to outcome, but there is scant literature on the relationship of patient perceived outcome and attributes of the pain clinic visit, including the patient interaction with the pain management specialist. The primary purpose of this study is to identify attributes of the patient-provider interaction most strongly associated with patient perceived outcome of their clinic visit. The secondary aim is to correlate patient perceived outcome with patient self-rated overall health. **METHODS:** A patient satisfaction survey conducted via phone approximately 3 weeks after the patient's pain clinic visit. **RESULTS:** The response rate was 60.2%; 987 patient surveys collected between 2006 and 2010 were used in the analysis. Four factors were significantly associated with the outcome: (1) Explanations by the physician of the patient's condition and treatment, (2) clear instructions regarding post-appointment activities, (3) knowing the patient as a person, and (4) the patient's self-rated health. In terms of the secondary objective, those who answered very good/excellent regarding their self-rated health had an 87% increased odds of better (very good/excellent) outcome of their pain clinic visit (or 1.87 times the odds of better outcome) compared with those who answered poor/fair/good. **CONCLUSIONS:** Our results suggest that pain physicians may positively impact patient perceived outcomes of clinic visits by explaining the patient's condition and treatment, providing instructions, and taking the time to understand the patients and their values.

### **Contrasting tensions between patients and PCPs in chronic pain management: a qualitative study.**

Bergman AA, Matthias MS, Coffing JM, Krebs EE

Pain Med. 2013 Jul 19. doi: 10.1111/pme.12172. [Epub ahead of print]

**OBJECTIVE:** With greater scrutiny on primary care providers' (PCPs) approaches to chronic pain management, more research is needed to clarify how concerns and uncertainties about opioid therapy affect the ways both patients with chronic pain and PCPs experience primary care interactions. The goal of this qualitative study was to develop a better understanding of the respective experiences, perceptions, and challenges that patients with chronic pain and PCPs face communicating with each other about pain management. **DESIGN:** Purposive and snowball sampling techniques were used to identify 14 PCPs. Patients who received  $\geq 6$  opioid prescriptions during the prior year were selected at random from the panels of participating physicians. Face-to-face in-depth interviews were conducted individually with patients and PCPs. **SETTING:** VISA 11 Roudebush VA Medical Center (RVAMC) in Indianapolis, Indiana. **SUBJECTS:** Fourteen PCPs and 26 patients with chronic pain participated. **METHODS:** An inductive thematic analysis was conducted separately with patient and PCP interview data, after which the emergent themes for both groups were compared and contrasted.



**RESULTS:** Three notable tensions between patients and PCPs were discovered: 1) the role of discussing pain versus other primary care concerns, 2) acknowledgment of pain and the search for objective evidence, and 3) recognition of patient individuality and consideration of relationship history. **CONCLUSIONS:** Competing demands of primary care practice, differing beliefs about pain, and uncertainties about the appropriate place of opioid therapy in chronic pain management likely contributed to the identified tensions. Several clinical communication strategies to help PCPs mitigate and manage pain-related tensions are discussed.

**Patients as collaborators: using focus groups and feedback sessions to develop an interactive, web-based self-management intervention for chronic pain.**

Moore SK, Guarino H, Acosta MC, Aronson ID, Marsch LA, Rosenblum A, Grabinski MJ, Turk DC  
Pain Med. 2013 Jul 16. doi: 10.1111/pme.12200. [Epub ahead of print]

**OBJECTIVES:** To describe the development of an interactive, web-based self-management intervention for opioid-treated, chronic pain patients with aberrant drug-related behavior. **METHODS:** Fifty-three chronic pain patients participated in either focus groups (N = 23) or individual feedback sessions (N = 30). Focus groups probed interest in and relevance of the planned content and structure of the program. Individual session participants reviewed draft program modules and provided feedback on acceptability, ease of use, and usefulness. Focus group transcripts were thematically analyzed, and summary statistics were performed on feedback data. **RESULTS:** Focus group participants stressed the need for additional pain management strategies and emphasized themes consistent with planned program content related to: 1) ambivalence about opioids; 2) reciprocal relationships among cognition, mood, and pain; 3) importance of recognizing physical limitations; and 4) effectiveness of goal setting for increasing motivation and functioning. Participants also offered insights on: 5) the loss of identity due to chronic pain; and 6) the desire to connect with pain peers to share strategies for managing daily life. Feedback session data demonstrate that participants believed that a web-based tool would be potentially useful and acceptable, and that exposure to program sections significantly increased participants' knowledge of key topics related to self-management of chronic pain. **CONCLUSIONS:** Results suggest the potential value of self-management for chronic pain patients and the potential acceptability of web-based delivery of intervention content. Focus group and feedback methodologies highlight the usefulness of including potential program users in intervention development.

**The capsaicin 8% patch for neuropathic pain in clinical practice: A retrospective analysis.**

Wagner T, Poole C, Roth-Daniek A  
Pain Med. 2013 May 24. doi: 10.1111/pme.12143. [Epub ahead of print]

**OBJECTIVE:** To investigate the response of patients with peripheral neuropathic pain (PNP) to capsaicin 8% patch treatment in a clinical setting. **DESIGN:** Retrospective analysis. **SETTING:** The Clinic for Pain Therapy and Palliative Medicine at the Medical Centre for the region of Aachen, Germany. **SUBJECTS:** Patients diagnosed with PNP who attended the clinic for capsaicin 8% patch treatment between January 13, 2010 and February 7, 2011. **OUTCOME MEASURES:** Pain intensity was assessed using the Numeric Pain Rating Scale (NPRS) at baseline and following each capsaicin 8% patch treatment. Changes in prescribed concomitant neuropathic pain (NP) medications and response duration were recorded. **RESULTS:** Overall, 68 patients with PNP conditions, including facial neuropathy (severe trigeminal neuralgia in V2), polyneuropathy, post-herpetic neuralgia, and mononeuropathies, received 96 treatments with the capsaicin 8% patch. The 53 patients with a follow-up of  $\geq 8$  weeks demonstrated a 48.4% mean reduction in NPRS score from baseline to Weeks 1-8. Among the 37 responders (those exhibiting  $\geq 30\%$  reduction in NPRS score from baseline to Weeks 1-8), the median time to re-treatment was 125 days. Following treatment, there was a significant ( $P < 0.001$ ) 54% reduction in the mean number of prescribed concomitant NP medications taken by patients. **CONCLUSIONS:** This analysis demonstrates that in clinical practice, the capsaicin 8% patch provides rapid and sustained pain reductions in patients with a variety of PNP conditions and a significant reduction in prescribed concomitant NP medications. The capsaicin 8% patch can be a valuable addition to the NP treatment armory for certain patients.

### **Sex differences in the medical care of VA patients with chronic non-cancer pain.**

Weimer MB, Macey TA, Nicolaidis C, Dobscha SK, Duckart JP, Morasco BJ  
Pain Med. 2013 Jun 26. doi: 10.1111/pme.12177. [Epub ahead of print]

**OBJECTIVE:** Despite a growing number of women seeking medical care in the veterans affairs (VA) system, little is known about the characteristics of their chronic pain or the pain care they receive. This study sought to determine if sex differences are present in the medical care veterans received for chronic pain. **DESIGN:** Retrospective cohort study using VA administrative data. **SUBJECTS:** The subjects were 17,583 veteran patients with moderate to severe chronic non-cancer pain treated in the Pacific Northwest during 2008. **METHODS:** Multivariate logistic regression assessed for sex differences in primary care utilization, prescription of chronic opioid therapy, visits to emergency departments for a pain-related diagnosis, and physical therapy referral. **RESULTS:** Compared with male veterans, female veterans were more often diagnosed with two or more pain conditions, and had more of the following pain-related diagnoses: fibromyalgia, low back pain, inflammatory bowel disease, migraine headache, neck or joint pain, and arthritis. After adjustment for demographic characteristics, pain diagnoses, mental health diagnoses, substance use disorders, and medical comorbidity, women had lower odds of being prescribed chronic opioid therapy (adjusted OR [AOR] 0.67, 95% CI 0.58-0.78), greater odds of visiting an emergency department for a pain-related complaint (AOR 1.40, 95% CI 1.18-1.65), and greater odds of receiving physical therapy (AOR 1.19, 95% CI 1.05-1.33). Primary care utilization was not significantly different between sexes. **CONCLUSIONS:** Sex differences are present in the care female veterans receive for chronic pain. Further research is necessary to understand the etiology of the observed differences and their associations with clinical outcomes.

### **Sex differences in pain: a brief review of clinical and experimental findings.**

Bartley EJ, Fillingim RB

Br J Anaesth. 2013 Jul;111(1):52-8. doi: 10.1093/bja/aet127.

Recent years have witnessed substantially increased research regarding sex differences in pain. The expansive body of literature in this area clearly suggests that men and women differ in their responses to pain, with increased pain sensitivity and risk for clinical pain commonly being observed among women. Also, differences in responsivity to pharmacological and non-pharmacological pain interventions have been observed; however, these effects are not always consistent and appear dependent on treatment type and characteristics of both the pain and the provider. Although the specific aetiological basis underlying these sex differences is unknown, it seems inevitable that multiple biological and psychosocial processes are contributing factors. For instance, emerging evidence suggests that genotype and endogenous opioid functioning play a causal role in these disparities, and considerable literature implicates sex hormones as factors influencing pain sensitivity. However, the specific modulatory effect of sex hormones on pain among men and women requires further exploration. Psychosocial processes such as pain coping and early-life exposure to stress may also explain sex differences in pain, in addition to stereotypical gender roles that may contribute to differences in pain expression. Therefore, this review will provide a brief overview of the extant literature examining sex-related differences in clinical and experimental pain, and highlights several biopsychosocial mechanisms implicated in these male-female differences. The future directions of this field of research are discussed with an emphasis aimed towards further elucidation of mechanisms which may inform future efforts to develop sex-specific treatments.

### **The influence of patient's sex, race and depression on clinician pain treatment decisions.**

Hirsh AT, Hollingshead NA, Bair MJ, Matthias MS, Wu J, Kroenke K

Eur J Pain. 2013 Jun 30. doi: 10.1002/j.1532-2149.2013.00355.x. [Epub ahead of print]

**BACKGROUND:** Pain treatments often vary across patients' demographic and mental health characteristics. Most research on this topic has been observational, has focused on opioid therapy exclusively and has not examined individual differences in clinician decision-making. The current study examined the influence of patient's sex, race and depression on clinicians' chronic pain treatment decisions. **METHODS:** We used virtual human technology and lens model methodology to enhance study realism and facilitate a richer understanding of treatment decisions. Clinicians and trainees (n = 100) made treatment decisions (opioid, antidepressant, pain specialty referral, mental health referral) for

16 computer-simulated patients with chronic low back pain. Patients' sex, race and depression status were manipulated across vignettes (image and text). RESULTS: Individual- and group-level analyses indicated that patient's depression status had the strongest and most consistent influence on treatment decisions. Although less influential overall, patient's sex and race were significantly influential for a subset of participants. Furthermore, the results indicated that participants who were influenced by patient's race had less experience in treating chronic pain than those who were not influenced by patient's race [ $t(11.59) = 4.75$ ;  $p = 0.001$ ;  $d = 1.20$ ]. CONCLUSIONS: The results of this study indicated considerable variability in participants' chronic pain treatment decisions. These data suggest that interventions to reduce variability in treatment decision-making and improve pain care should be individually tailored according to clinicians' decision profiles.

## **Vulvovaginal Disorders**

### **Assessment of women's sexual health using a holistic, patient-centered approach.**

Zielinski RE

J Midwifery Womens Health. 2013 May;58(3):321-7. doi: 10.1111/jmwh.12044.

Sexual health problems are common in women and have the potential to affect all aspects of their lives. These issues can include diminished or lack of desire for sex, difficulty with arousal and sexual pleasure, inability to orgasm, and pain with sex. Causes of sexual health issues can be complex and multifaceted; therefore, a holistic perspective, in which all potential factors are considered, is warranted. Despite the prevalence of women's sexual health issues, discussion by providers is often absent or limited to avoidance of sexually transmitted infections or unwanted pregnancies. Health care providers may feel they do not have the time or resources to address sexual health problems. This article provides a sexual health assessment approach using a model of sexual health whereby sociocultural factors are given priority, followed by factors related to partner and relationships, psychological factors, and finally medical factors.

### **Dyspareunia and vaginal bleeding associated with isotretinoin: a rare complication.**

Oguz Topal I

J Sex Med. 2013 Jul 11. doi: 10.1111/jsm.12259

No abstract listed.

### **Vulvovaginal candidiasis as a chronic disease: Diagnostic criteria and definition.**

Hong E, Dixit S, Fidel PL, Bradford J, Fischer G

J Low Genit Tract Dis. 2013 Jun 11. [Epub ahead of print]

OBJECTIVE: Although recurrent vulvovaginal candidiasis is defined as 4 or more discrete attacks of vulvovaginal candidiasis per year, there is no diagnostic nomenclature or definition for the many women who are chronically symptomatic. This study aims to establish and propose a definition and a set of diagnostic criteria, which would enable clinicians to promptly identify and treat women with chronic vulvovaginal candidiasis (CVVC). DESIGN: Prospective cohort study. SETTING: Public and private vulvar dermatology outpatient clinics in Sydney, Australia. PARTICIPANTS: Data were obtained prospectively from 50 women with presumptive CVVC and 42 controls. Historical and clinical features of CVVC identified by expert consensus were compared between the 2 groups. Diagnostic criteria were then prospectively applied to a further 163 patients to verify their accuracy. OUTCOME MEASURES: Signs and symptoms diagnostic of CVVC. RESULTS: The following characteristics were found to be significantly more common in women with CVVC compared to controls ( $p \leq .001$ ): a history of positive vaginal Candida swab, discharge, dyspareunia, soreness, swelling, cyclicity, and exacerbation of symptoms with antibiotics. CONCLUSIONS: We propose that CVVC can be confidently diagnosed using the major criteria of a chronic nonspecific and nonerosive vulvovaginitis that includes at least 5 or more properties from the following criteria: soreness, dyspareunia, positive vaginal swab either at

presentation or in the past, previous response to antifungal medication, exacerbation with antibiotics, cyclicity, swelling, and discharge. This condition responds reliably to oral antifungal medication.

#### **Evaluation of *Syngonanthus nitens* (Bong.) Ruhl. extract as antifungal and in treatment of vulvovaginal candidiasis.**

de Freitas Araújo MG, Pacífico M, Vilegas W, Dos Santos LC, Icely PA, Miró MS, Scarpa MV, Bauab TM, Sotomayor CE  
Med Mycol. 2013 Jun 13. [Epub ahead of print]

The purpose of this study was to evaluate the in vitro anticandidal activity of a methanolic extract of *Syngonanthus nitens* scapes against different *Candida* species and clinical isolates from patients with vulvovaginal candidiasis (VVC), and its effect in vivo in the treatment of vaginal infection. Chemical characterization of the extract was performed by HPLC-UV analyses and showed the presence of flavones derivatives. The extract was effective against several *Candida* strains from our collection and species recovered from VVC patients, and was able to inhibit the yeast-hyphal transition. No cytotoxic activity against human female reproductive tract epithelial cells and no hemolytic activity against human red blood cells were observed. In the in vivo model of VVC, we evaluated the efficacy of the intravaginal treatment with a cream containing the extract at doses of 0.5, 1.0 and 2.0%. The treatment eradicated the vaginal fungal burden in infected rats after 8 days of treatment. *S. nitens* extract could be considered as an effective and non-toxic natural antifungal agent in the treatment of vulvovaginal candidiasis.

#### **Immune deviation in recurrent vulvovaginal candidiasis: correlation with iron deficiency anemia.**

Naderi N, Etaati Z, Rezvani Joibari M, Sobhani SA, Hosseini Tashnizi S  
Iran J Immunol. 2013 Jun;10(2):118-26. doi: 10.1016/j.ijiv.2013.06.007

**BACKGROUND:** Iron Deficiency Anemia (IDA) has been controversially linked to IL-4 production in previous studies. A predominant Th1 response leads to resistance against recurrent vulvovaginal candidiasis (RVVC), whereas a Th2 response exacerbates the disease. **OBJECTIVE:** To investigate the possible effect of iron deficiency on the host's susceptibility to RVVC as a result of the Th1/Th2 cytokine polarization. **METHODS:** We conducted a case-control study of 92 women in 4 groups based on strict inclusion and exclusion criteria: RVVC+IDA+ group consisted of 23 women with RVVC and IDA; RVVC+ IDA- group consisted of 23 women with RVVC without IDA; RVVC-IDA+ group consisted of 23 women without RVVC and with IDA and RVVC- IDA- group consisted of 23 healthy women. The iron parameters and key cytokines (IFN- $\gamma$ , IL-10, IL-12, IL-4) were measured in blood samples. **RESULTS:** Comparison of IL-4 production between RVVC+ IDA+ ( $12.2 \pm 1.3$  pg/ml) and RVVC+ IDA- ( $2.4 \pm 4.0$  pg/ml) groups ( $p=0.044$ ), between RVVC- IDA+ ( $14.6 \pm 1.7$  pg/ml) and RVVC- IDA- ( $1.28 \pm 3.6$  pg/ml) groups ( $p=0.006$ ), between RVVC- IDA+ ( $14.6 \pm 1.7$  pg/ml) and RVVC+ IDA- ( $2.4 \pm 4.0$  pg/ml) groups ( $p=0.009$ ) and also between RVVC+ IDA+ and RVVC- IDA- ( $1.28 \pm 3.6$  pg/ml) groups ( $p=0.03$ ) showed significant differences. We found a significant positive correlation between IL-4 and total iron binding capacity (TIBC,  $p=0.046$ ) and between serum IL-10 and Hb levels ( $p=0.041$ ) in the RVVC+ IDA- group. There was also a significant negative correlation between serum IL-4 and levels of serum iron (SI,  $p=0.041$ ) in the RVVC- IDA- group. **CONCLUSION:** It seems that IDA determines the balance between and the intensity of Th1 and Th2 arms of the immune response and leads to a deviation toward Th2 response, which could contribute to recurrence of candidiasis.

#### **IL-22 and IDO1 affect immunity and tolerance to murine and human vaginal candidiasis.**

De Luca A, Carvalho A, Cunha C, Iannitti RG, Pitzurra L, Giovannini G, Mencacci A, Bartolommei L, Moretti S, Massi-Benedetti C, Fuchs D, De Bernardis F, Puccetti P, Romani L  
PLoS Pathog. 2013 Jul;9(7):e1003486. doi: 10.1371/journal.ppat.1003486. Epub 2013 Jul 11.

The ability to tolerate *Candida albicans*, a human commensal of the gastrointestinal tract and vagina, implicates that host defense mechanisms of resistance and tolerance cooperate to limit fungal burden and inflammation at the different body sites. We evaluated resistance and tolerance to the fungus in experimental and human vulvovaginal candidiasis (VVC) as well as in recurrent VVC (RVVC). Resistance and tolerance mechanisms were both activated in murine VVC, involving IL-22 and IL-10-producing regulatory T cells, respectively, with a major contribution by the enzyme indoleamine 2,3-dioxygenase 1 (IDO1). IDO1 was responsible for the production of tolerogenic kynurenines,

such that replacement therapy with kynurenines restored immunoprotection to VVC. In humans, two functional genetic variants in IL22 and IDO1 genes were found to be associated with heightened resistance to RVVC, and they correlated with increased local expression of IL-22, IDO1 and kynurenines. Thus, IL-22 and IDO1 are crucial in balancing resistance with tolerance to *Candida*, their deficiencies are risk factors for RVVC, and targeting tolerance via therapeutic kynurenines may benefit patients with RVVC.

#### **Genetic susceptibility to *Candida* infections.**

Smeekens SP, van de Veerdonk FL, Kullberg BJ, Netea MG  
EMBO Mol Med. 2013 Jun;5(6):805-13. doi: 10.1002/emmm.201201678.

*Candida* spp. are medically important fungi causing severe mucosal and life-threatening invasive infections, especially in immunocompromised hosts. However, not all individuals at risk develop *Candida* infections, and it is believed that genetic variation plays an important role in host susceptibility. On the one hand, severe fungal infections are associated with monogenic primary immunodeficiencies such as defects in STAT1, STAT3 or CARD9, recently discovered as novel clinical entities. On the other hand, more common polymorphisms in genes of the immune system have also been associated with fungal infections such as recurrent vulvovaginal candidiasis and candidemia. The discovery of the genetic susceptibility to *Candida* infections can lead to a better understanding of the pathogenesis of the disease, as well as to the design of novel immunotherapeutic strategies. This review is part of the review series on host-pathogen interactions. See more reviews from this series.

#### **Association of pregnancy and *Candida* vaginal colonization in women with or without symptoms of vulvovaginitis.**

Leli C, Mencacci A, Meucci M, Bietolini C, Vitali M, Farinelli S, D'alò F, Bombaci JC, Perito S, Bistoni F  
Minerva Ginecol. 2013 Jun;65(3):303-9.

**AIM:** *Candida* infection is one of the main causes of vulvovaginitis. The experience of symptoms of vulvovaginitis during pregnancy changes in relation to clinical, behavioral, and demographic factors. Candidiasis is associated with an increased risk of delivery complications. In some studies pregnant women are found more symptomatic than non-pregnant women, but in others a higher prevalence of asymptomatic infections is described during pregnancy. The aims of this study were to evaluate the prevalence of *Candida* vaginal colonization in pregnant women, and investigate if the occurrence of symptoms is influenced by pregnancy, in a population of Italian native and immigrant women. **METHODS:** A total of 344 outpatients, who visited the laboratory for routine genital examination, independently of pregnancy or presence or absence of symptoms of vulvovaginitis, were evaluated. **RESULTS:** Colonization by *Candida* spp. was significantly higher in pregnant than non-pregnant patients (31.4% vs. 19.9%;  $\chi^2=5.59$ ;  $P=0.018$ ), nevertheless pregnant women were significantly more often asymptomatic compared to non-pregnant (46.5% vs. 16%;  $\chi^2=42.31$ ;  $P<0.0001$ ). In the sub-group of women colonized by *Candida* spp., pregnancy resulted significantly associated to asymptomatic infection (58.1% vs. 30.8%;  $\chi^2 =6.18$ ;  $P=0.013$ ). A binary logistic regression analysis showed pregnancy or lactobacilli colonization independently associated to a lower probability of experiencing symptoms of vulvovaginitis (respectively:  $P<0.0001$  and  $P=0.008$ ). **CONCLUSION:** Pregnancy seems to be independently associated to *Candida* spp. asymptomatic vaginal infection. Given that candidiasis has been associated with possible delivery complications, these results suggest to screen for *Candida* spp. vaginal colonization asymptomatic women during pregnancy.

#### **Superimposed methicillin-resistant *Staphylococcus aureus* infection of vulvar eczematous dermatitis: a case report.**

Carey E, Zedek D, Lewis J, Zolnoun D  
J Reprod Med. 2013 May-Jun;58(5-6):261-3.

**BACKGROUND:** Vulvar eczematous dermatitis predisposes patients to superimposed infections, which may result in late diagnosis and architectural destruction. Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is on the rise in genitalia and lower extremities. **CASE:** A 44-year-old woman presented with recurrent vulvar lesions and pain. A diagnosis of MRSA in the setting of eczema was achieved with concomitant use of photography and dermatopathologic review. Antibiotics were tailored to the resistant infection and preventative moisturization therapy was utilized.

**CONCLUSION:** Awareness of dermatologic conditions affecting the vulva is principal in routine gynecologic care. Barrier protection of eczematous vulvar skin may prevent superficial infections. The regular use of photographic documentation and dermatopathology may decrease time to diagnosis with infrequent or rare conditions.

**Lichen sclerosus in children and adolescents.**

Dendrinios ML, Quint EH

Curr Opin Obstet Gynecol. 2013 Jun 27. [Epub ahead of print]

**PURPOSE OF REVIEW:** This review of lichen sclerosus in children and adolescents will discuss the disease and highlight the most recent literature. **RECENT FINDINGS:** Lichen sclerosus continues to be poorly recognized and misdiagnosed by clinicians. There is growing support for an autoimmune component in the cause of this disease. Recent studies confirm that lichen sclerosus does not resolve after puberty but usually improves. In small case series, topical calcineurin inhibitors are effective as second-line therapy. **SUMMARY:** Lichen sclerosus is an uncommon, poorly recognized disease in girls and adolescents and is likely to have a chronic course requiring long-term follow-up and treatment. There needs to be increased awareness among providers of this disease as a cause of vulvar itching. Because of the lack of knowledge of the natural course and treatment outcomes, prospective, multicenter studies are needed.

**Mometasone fuoroate 0.1% ointment in the treatment of vulvar lichen sclerosus: a study of efficacy and safety on a large cohort of patients.**

Virgili A, Borghi A, Minghetti S, Corazza M

J Eur Acad Dermatol Venereol. 2013 Jul 23. doi: 10.1111/jdv.12219. [Epub ahead of print]

**BACKGROUND:** Guidelines identify a 3-month topical application of an ultra-potent corticosteroid ointment as the mainstay of medical treatment for vulvar lichen sclerosus (VLS). However, there are no trials providing evidence that any specific corticosteroid is superior to another. **OBJECTIVE:** To assess the effectiveness and safety of a 12-week application of mometasone fuoroate (MMF) 0.1% ointment, with a tapering regimen, in achieving control of VLS signs and symptoms and to detect potential risk factors for VLS non-response. **METHODS:** 147 patients affected with VLS were enrolled in a 12-week active treatment phase (ATP) with topical 0.1% MMF. The primary efficacy endpoint was the rate of patients achieving clinical response, as defined by protocol parameters. The secondary efficacy endpoint was to assess the changes of mean VLS-related symptoms after the 12-week ATP compared with baseline. **RESULTS:** By the end of the ATP, 113 patients (80.7%) experienced a treatment response, whereas 27 women (19.3%) were judged as non-responders. Mean symptom scores decreased significantly in the study patients, regardless of their clinical response at the end of the ATP. Among all the epidemiological and clinical data considered, only the absence of previous medical therapies was found to be related to a significantly higher risk of non-response to treatment. **CONCLUSIONS:** Application of 0.1% MMF ointment for 12 weeks on a tapering regimen was found to be an effective and safe therapy option in the ATP of VLS and could represent an alternative first-line treatment to an ultra-potent molecule.

**Long-term follow-up of women with genital lichen sclerosus.**

[No authors listed]

Menopause Int. 2013 May 3. [Epub ahead of print]

No abstract available. Free full text online.

**Ovarian adult granulosa cell tumor and vulval lichenoid inflammation.**

Hansen MH, Jeppesen U, Johansen T

Acta Obstet Gynecol Scand. 2013 Jun 5. doi: 10.1111/aogs.12191. [Epub ahead of print]

Mucocutaneous conditions such as dermatomyositis have been found to be associated with malignant ovarian disease (1, 2). We call attention to a possible association between ovarian adult granulosa cell tumor (AGCT) and lichenoid

inflammation through the case of a 65 year old woman whose lichenoid eruption in the vulva disappeared after treatment of AGCT. The patient was hospitalized due to lower abdominal pain attributed to diverticulitis, treated with antibiotics, and in the diagnostic process an ultrasound of the pelvic organs was performed. The ovaries showed no pathology, but the endometrium was thickened, suggesting raised estrogen levels.

**Superimposed methicillin-resistant *Staphylococcus aureus* infection of vulvar eczematous dermatitis: a case report.**

Carey E, Zedek D, Lewis J, Zolnoun D

J Reprod Med. 2013 May-Jun;58(5-6):261-3.

**BACKGROUND:** Vulvar eczematous dermatitis predisposes patients to superimposed infections, which may result in late diagnosis and architectural destruction. Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is on the rise in genitalia and lower extremities. **CASE:** A 44-year-old woman presented with recurrent vulvar lesions and pain. A diagnosis of MRSA in the setting of eczema was achieved with concomitant use of photography and dermatopathologic review. Antibiotics were tailored to the resistant infection and preventative moisturization therapy was utilized. **CONCLUSION:** Awareness of dermatologic conditions affecting the vulva is principal in routine gynecologic care. Barrier protection of eczematous vulvar skin may prevent superficial infections. The regular use of photographic documentation and dermatopathology may decrease time to diagnosis with infrequent or rare conditions.

**A clinicopathologic study of labia minora hypertrophy: Signs of localized lymphedema were universal.**

Barrett MM, Carlson JA

J Low Genit Tract Dis. 2013 Jun 11. [Epub ahead of print]

**OBJECTIVE:** To describe the clinical and pathologic features of women undergoing labioplasty for labia minora hypertrophy (LH) and to determine whether localized lymphedema plays a role in its pathogenesis. **MATERIALS AND METHODS:** A retrospective case series of consecutive cases of labioplasties performed for LH was retrieved from a 10-year period. Clinical, histopathologic, and immunohistochemical features were evaluated. **RESULTS:** Thirty-four labioplasty specimens from 31 women were identified. The women had a median/mean age of 36/35 years (range = 14-62 y) and had noted the presence of LH for a median/mean period of 36/86 months (range = 5-264 mo). A minority of patients had antecedent vaginal delivery (29%) and vulvar trauma (12%) and were either overweight (20%) or obese (27%). About half complained of vulvar appearance and approximately a third each had symptoms of pain, dyspareunia, or irritation. After a median/mean follow-up time of 40/44 months, 3 patients had recurrent LH (9%). The volume of excised tissue was greater for the patients with recurrent LH, than those without (mean of 9.8 vs 5.6 mL, respectively); however, no clinicopathologic finding predicted recurrence of LH. Histopathologically, all LH specimens showed diagnostic signs of chronic lymphedema, and compared with vulvar controls, LH had a significantly greater number of lymphangiectases (mean 15/mm vs 3/mm,  $p = .001$ ) and showed greater mean maximal lymphatic dilation (0.12 vs 0.04 mm,  $p = .004$ ), respectively. In addition, lichenification (94%), indicating chronic irritation, and sebaceous hyperplasia (60%), perisebaceous inflammation, and *Demodex folliculorum* infestation (3%), a constellation of findings commonly seen in phymatous rosacea, were evident. **CONCLUSIONS:** Rather than an anatomic variant, LH seems to be a manifestation of chronic lymphedema, either acquired or primary with delayed onset. Because persistent lymphedema can lead to functional debilitation, recurrent skin infections, elephantiasis, and, rarely, malignancy, early excision and treatment of factors that promote lymphedema would be effective management of this rare condition.

**Application and tolerability of Herpotherm(®) in the treatment of genital herpes.**

Schlippe G, Voss W, Brenn LC

Clin Cosmet Investig Dermatol. 2013 Jun 5;6:163-6. doi: 10.2147/CCID.S41145. Print 2013.

Genital herpes is the manifestation of a herpes simplex virus 2 infection. Standard treatment uses both local and systemic approaches. Here, we report on the results of a local therapy approach with 31 female patients at a gynecological practice. In the here-described approach, established genital herpes infection was treated with the medical device Herpotherm(®), with or without virostatic drugs. Herpotherm(®) is a certified medical device operating

on the basis of local heat application. Parameters evaluated during the approach were (i) subjective patient assessments and (ii) objective assessment of the physician. In the described therapy approach a positive effect in terms of nature and severity in the course of the disease using Herpotherm(®) could be demonstrated. It could be shown that Herpotherm(®) can also be used for genital herpes and that it is well tolerated. In relation to other therapies using topical treatment for genital herpes, an extremely rapid reduction of pain and herpetic symptoms could be observed. Intolerances or discontinued use as a result of complications were not observed.

#### **Vulvar pyoderma gangrenosum originating from a healed obstetric laceration.**

Reed BG, Shippey S, Kremp A, Belin E

Obstet Gynecol. 2013 Aug;122(2 Pt 2):452-5. doi: 10.1097/AOG.0b013e318297e98f.

**BACKGROUND:** Pyoderma gangrenosum is a rare dermatologic disorder that can occur on the vulva. **CASE:** A 25-year-old woman, gravida 2 para 1 abortus 1, had development of pain and subsequent ulceration at the location of her previously healed vulvar obstetric laceration. The ulceration and pain continued to worsen despite wound management. Once the diagnosis of vulvar pyoderma gangrenosum was made, cyclosporine was started and the wound rapidly healed. **CONCLUSION:** Vulvar pyoderma gangrenosum should be considered when a vulvar wound is not healing with conservative measures. Cyclosporine can be considered as an alternative to steroids for treatment.

#### **Two case presentations of profound labial edema as a presenting symptom of hypermobility-type Ehlers-Danlos syndrome.**

Krapf JM, Goldstein AT

J Sex Med. 2013 Jul 22. doi: 10.1111/jsm.12229. [Epub ahead of print]

**INTRODUCTION:** Hypermobility-type Ehlers-Danlos syndrome (EDS), an often-missed diagnosis with the potential for serious sequelae, may have a variety of uncommon presentations, some of which may be gynecologic. **AIM:** The aim of this case report is to present two cases of profound labial edema associated with intercourse as a presenting symptom of hypermobility-type EDS. **METHODS:** A 25-year-old female presented with severe labia minora swelling and bladder pressure associated with intercourse, in addition to persistent genital arousal. History revealed easy bruising, joint pain, and family history of aneurysm. A 22-year-old female presented with intermittent profound labial swelling for 6 years, associated with sensitivity and pain with intercourse. The patient has a history of joint pain and easy bruising, as well as a sister with joint hypermobility and unexplained lymphedema. The presenting symptom of profound labial edema led to the diagnosis of hypermobility-type EDS. **RESULTS:** Patients with hypermobility syndrome exhibit an increased ratio of type III collagen to type I collagen, causing tissue laxity and venous insufficiency. Abnormal collagen may lead to gynecologic manifestations, including unexplained profound labial edema, pelvic organ prolapse in the absence of risk factors, and possibly persistent genital arousal. **CONCLUSIONS:** This case report highlights the need for further research to determine incidence of labial edema in hypermobility-type EDS and to further elucidate a potential correlation between profound labial edema and collagen disorders.

#### **Vulvar swelling, plaques, and nodules in a young adult woman.**

Li SL, Li C

JAMA. 2013 Jun 26;309(24):2596-7. doi: 10.1001/jama.2013.7080.

No abstract available.



### **Photodynamic therapy with M-ALA as non-surgical treatment option in patients with primary extramammary Paget's disease.**

Fontanelli R, Papadia A, Martinelli F, Lorusso D, Grijuela B, Merola M, Solima E, Ditto A, Raspagliesi F  
Gynecol Oncol. 2013 Jul;130(1):90-4. doi: 10.1016/j.ygyno.2013.04.008.

**INTRODUCTION:** Extramammary Paget disease (EMPD) is a rare neoplasm of the skin that presents with erythematous or leukoplacic plaques causing pruritus and pain. Standard treatment is surgical but local failures and recurrences are frequent, leading to multiple mutilating surgeries. Aim of the study is to evaluate the effectiveness of photodynamic therapy (PDT) to obtain a clinical response and symptom control with a non surgical approach in these patients. **MATERIALS AND METHODS:** After disease extension evaluation and symptoms assessment women with EMPD were prospectively treated with aminolevulinic-acid methyl-ester (M-ALA) PDT. Clinical and symptoms response were evaluated after 3cycles and after any further PDT. **RESULTS:** Thirty-two patients with vulvar EMPD underwent M-ALA PDT. In sixteen (50%) patients the lesion extended to the perineal and/or perianal area. After three courses of treatment, three patients (9.4%) had a complete resolution of the symptoms; 25 patients (78.1%) a partial resolution and a stable disease was recorded in four patients (12.5%). None of the patients had progression of disease. Both size of the lesion and EMPD associated symptoms decreased significantly after three courses of treatment. Eighteen patients (56.2%) recurred and 16 (88.9%) were treated with further PDT. Among the 26 patients who underwent a further PDT, 16 patients (61.5%) achieved at least a partial response. **CONCLUSION:** M-ALA PDT even if not curative is a reliable strategy to control EMPD and its associated symptoms even in an outpatient setting. M-ALA PDT is able to control large and multiple lesions regardless of the area involved, preserving cosmetic and/or functional anatomy.

### **Electrochemotherapy can be used as palliative treatment in patients with repeated loco-regional recurrence of squamous vulvar cancer: a preliminary study.**

Perrone AM, Galuppi A, Cima S, Pozzati F, Arcelli A, Cortesi A, Procaccini M, Pellegrini A, Zamagni C, De Iaco P  
Gynecol Oncol. 2013 Jun 28. doi: 10.1016/j.ygyno.2013.06.028. [Epub ahead of print]

**OBJECTIVE:** Electrochemotherapy (ECT) is an attractive treatment for solid cutaneous tumours with a good response rate (55-92%). No studies have evaluated ECT performed in vulvar cancer. The aim of our study was to evaluate the safety, local tumour efficacy and relief of symptoms of ECT treatment in patients affected by recurrence of squamocellular vulvar cancer (V-SCC) unsuitable for standard treatments. **METHODS:** We enrolled nine patients with histological diagnosis of recurrence of V-SCC. Intravenous bleomycin was injected under general sedation after an accurate mapping of all lesions and ECT was performed. Patients were reviewed after one, three and six months. Response to therapy was evaluated using RECIST criteria and quality of life (QoL) was evaluated via questionnaires. **RESULTS:** The median age was 84 years (range 80-90years). The main location of recurrences was the vulva (87.5%). Multiple lesions were present in 25% of cases. No peri-operative complications were observed. Response to therapy was complete in 62.5% of patients, partial in 12.5%, no change was observed in 12.5% and progression of disease in 12.5% of patients respectively. Evaluation of symptoms showed a significant reduction of pain, bleeding, odour ( $p<0.04$ ) and urinary discomfort ( $p<0.04$ ). We observed two relapses at four and seven months after treatment. After nine months fifty percent of patients were alive. **CONCLUSIONS:** Our preliminary study showed that ECT is a suitable procedure in elderly patients with loco-regional vulvar cancer relapses. ECT can be used as palliative therapy and the treatment relieves symptoms and improves QoL.

### **Anogenital malignancies and premalignancies: facts and controversies.**

Kutlubay Z, Engin B, Zara T, Tüzün Y  
Clin Dermatol. 2013 Jul-Aug;31(4):362-73. doi: 10.1016/j.clindermatol.2013.01.003.

Anogenital malignancies and premalignancies are an important personal/public health problem due to their effects on individuals' physical, mental, and sexual health. Also, due to their etiological association with human papillomavirus (HPV) infection, anogenital malignancies and premalignancies constitute an immense public health burden. In addition to HPV infection, immunosuppression, HIV infection, chronic dermatoses, such as lichen sclerosis, previous radiotherapy and chemotherapy treatments, and smoking, are the other important etiopathologic factors in the development of

anogenital malignancies and premalignancies. The incidence of anal squamous cell carcinoma (SCC) has increased considerably in the past decade, mainly due to the growing number of cases in high-risk groups, such as men who have sex with men, immunosuppressed individuals, and patients with HIV infection. Also, an increase in vulvar intraepithelial neoplasia (VIN) and VIN-related invasive vulvar cancer has been noted in women younger than age 50 years due to its association with HPV infections over the past decade. SCC of the scrotum seems to be the first cancer linked to occupational exposure. Bowen's disease, Bowenoid papulosis, and erythroplasia of Queyrat are the most widely seen premalignancies of anogenital region and are all forms of squamous intraepithelial neoplasia. Histopathologically, these conditions share identical histologic features of SCC in situ, but their clinical features differ. Early diagnosis is vital to improve prognosis, especially in anogenital malignancies. Also, if a delay occurs in diagnosis, treatment options used will be associated with significant negative effects on the patient's psychological well-being and quality of life; hence, management of anogenital malignancies and premalignancies should be organized in a multidisciplinary fashion.

### **Phosphorylated S6 as an immunohistochemical biomarker of vulvar intraepithelial neoplasia.**

Pinto AP, Degen M, Barron P, Crum CP, Rheinwald JG

Mod Pathol. 2013 Jun 14. doi: 10.1038/modpathol.2013.85. [Epub ahead of print]

As life expectancy lengthens, cases of non-viral-associated vulvar squamous cell carcinoma and its precursor lesion, so-called differentiated vulvar intraepithelial neoplasia (VIN), continue to increase in frequency. Differentiated VIN often is difficult to recognize and failure to detect it before invasion results in morbidity and mortality. Thus, identification of a reliable biomarker for this type of lesion would be of great clinical benefit. Our recent studies have identified activation (ser235/236 phosphorylation) of ribosomal protein S6 (p-S6) in basal epithelial cells as an event that precedes and accompanies laminin  $\gamma$ 2 overexpression in most preinvasive oral dysplasias. To test this as a potential biomarker of vulvar dysplasia, we immunostained seven differentiated VINs and nine papillomavirus-related 'classic' VINs, most of which were associated with carcinoma, for p-S6. All carcinomas, all differentiated VINs, and most classic VINs contained regions of p-S6 staining in the basal layer, whereas basal and parabasal cells of normal vulvar epithelium and hyperplastic and inflamed lesions lacking cellular atypia were p-S6 negative. Laminin  $\gamma$ 2 was expressed in a subset of VINs, always occurring within basal p-S6 positive regions, as we had found previously for oral dysplasias. Lichen sclerosis is considered a potential precursor of vulvar carcinoma. Two lichen sclerosis lesions of patients with a concurrent carcinoma and one of six lichen sclerosis lesions without atypia or known concurrent carcinoma were basal p-S6 positive. In summary, there is a distinct difference in p-S6 basal cell layer staining between benign and neoplastic vulvar squamous epithelium, with consistent staining of differentiated VIN and of some lichen sclerosis lesions. These results support further studies to assess the potential of p-S6 as a biomarker to identify vulvar lesions at risk of progressing to invasive cancer.

### **Prevention, identification and treatment of vulvar squamous (pre)malignancies: a review focusing on quality of care.**

van den Einden LC, van der Avoort IA, de Hullu JA

Expert Rev Anticancer Ther. 2013 Jul;13(7):845-59. doi: 10.1586/14737140.2013.811059.

Vulvar squamous cell carcinoma, its precursor lesions (usual and differentiated vulvar intraepithelial neoplasia) and lichen sclerosis are rare diseases that may have a large impact on the lives of affected women and their partners. Proper identification is vital, but the lesions are sometimes difficult to diagnose because of their rarity and variety of symptoms. High quality of care and proper treatment is important in order to minimize the morbidity and mortality caused by these lesions. This review gives an outline of the latest insights regarding the current evidence in this area and unresolved issues. Additionally, it highlights the improvements that should be made in order to optimize prevention and identification of (pre-)malignant vulvar lesions and to increase the quality of care for these patients.

### **Patterns of care for locally advanced vulvar cancer.**

Sharma C, Deutsch I, Herzog TJ, Lu YS, Neugut AI, Lewin SN, Chao CK, Hershman DL, Wright JD  
Am J Obstet Gynecol. 2013 Mar 15. doi: 10.1016/j.ajog.2013.03.013. [Epub ahead of print]

**OBJECTIVE:** Patients with locally advanced vulvar carcinoma can be treated with primary surgery or neoadjuvant chemoradiation. Neoadjuvant treatment appears to be associated with decreased morbidity and acceptable long-term outcomes. We examined the patterns of care for women with locally advanced vulvar cancer. **STUDY DESIGN:** Data from the Surveillance, Epidemiology, and End Results (SEER) database was used to examine women with stage III-IVA vulvar cancer treated from 1988 to 2008. Primary therapy was classified as surgery or radiation. Multivariable logistic regression models were developed to examine the use of primary radiotherapy. **RESULTS:** We identified a total of 2292 women including 1757 who underwent primary surgery (76.7%) and 535 treated with primary radiation (23.3%). The use of primary radiation increased with time from 18.0% in 1988 to 30.1% in 2008. In a multivariable model, older women (odds ratio [OR], 1.33; 95% confidence interval [CI], 1.03-1.72), black women (OR, 1.59; 95% CI, 1.14-2.23), and patients with stage IVA tumors (OR, 2.23; 95% CI, 1.78-2.81) were more likely to receive primary radiation. Among women treated with primary radiotherapy, only 17.8% ultimately underwent surgical resection. **CONCLUSION:** The use of primary radiation for locally advanced vulvar cancer is limited but has increased over time. Multiple patient and tumor factors influence use. The majority of patients with stage III-IVA vulvar cancer treated with primary radiation therapy did not undergo surgical resection.

### **Etiology of vulvar cancer will impact on treatment options and therapy outcome: Two major pathways of vulvar cancer.**

Regauer S, Reich O

Gynecol Oncol. 2013 Jul 16. doi: 10.1016/j.ygyno.2013.05.041. [Epub ahead of print]

No abstract available.

### **Report of two cases of adenoid cystic carcinoma of Bartholin's gland and review of literature.**

Hsu ST, Wang RC, Lu CH, Ke YM, Chen YT, Chou MM, Ho ES

Taiwan J Obstet Gynecol. 2013 Mar;52(1):113-6. doi: 10.1016/j.tjog.2012.10.005.

**OBJECTIVE:** Primary adenoid cystic carcinoma (ACC) of Bartholin's gland is a rare gynecologic malignancy. We report two cases from primary treatment to recurrence and the adjuvant treatment. **CASE REPORT:** A woman aged 37 years presented with a mass on the right posterior labia minor and underwent right radical hemi-vulvectomy and right-side inguino-femoral node dissection. Final pathology showed ACC arising from Bartholin's gland with positive margins. She received adjuvant external beam radiation to the pelvis, right vulva, and groin area. However, distal metastasis occurred 42 months after initial treatment and she eventually died of multiple metastases. Another woman aged 48 years presented with a mass on the right posterior labia with intermittent pain. She underwent right hemi-vulvectomy and right inguino-femoral lymph node dissection only because pathology showed ACC of Bartholin's gland with negative surgical margins. Lung metastasis occurred 59 months after initial treatment. She took tamoxifen only and achieved stable disease status for 4 years. **CONCLUSION:** To date, about 70 cases have been reported. We treated our second patient with antiestrogen therapy for 4 years and achieved good quality of life and stable disease status. However, further study on hormone therapy for ACC of Bartholin's gland is needed.

### **Female genital mutilation/cutting in The Gambia: long-term health consequences and complications during delivery and for the newborn.**

Kaplan A, Forbes M, Bonhoure I, Utzet M, Martín M, Manneh M, Ceesay H

Int J Womens Health. 2013 Jun 17;5:323-31. doi: 10.2147/IJWH.S42064. Print 2013.

**BACKGROUND:** Female genital mutilation/cutting (FGM/C) is a harmful traditional practice deeply rooted in 28 Sub-Saharan African countries. Its prevalence in The Gambia is 76.3%. The objective of this study was to gain precise

information on the long-term health consequences of FGM/C in The Gambia as well as on its impact on delivery and on the health of the newborns. METHODS: Data were collected from 588 female patients examined for antenatal care or delivery in hospitals and health centers of the Western Health Region, The Gambia. The information collected, both through a questionnaire and medical examination, included sociodemographic factors, the presence or not of FGM/C, the types of FGM/C practiced, the long-term health consequences of FGM/C, complications during delivery and for the newborn. Odds ratios, their 95% confidence intervals, and P values were calculated. RESULTS: The prevalence of patients who had undergone FGM/C was 75.6% (type I: 75.6%; type II: 24.4%). Women with type I and II FGM/C had a significantly higher prevalence of long-term health problems (eg, dysmenorrhea, vulvar or vaginal pain), problems related to anomalous healing (eg, fibrosis, keloid, synechia), and sexual dysfunction. Women with FGM/C were also much more likely to suffer complications during delivery (perineal tear, obstructed labor, episiotomy, cesarean, stillbirth) and complications associated with anomalous healing after FGM/C. Similarly, newborns were found to be more likely to suffer complications such as fetal distress and caput of the fetal head. CONCLUSION: This study shows that FGM/C is associated with a variety of long-term health consequences, that women with FGM/C are four times more likely to suffer complications during delivery, and the newborn is four times more likely to have health complications if the parturient has undergone FGM/C. These results highlight for the first time the magnitude of consequences during delivery and for the newborn, associated with FGM/C in The Gambia.