NVA Research Update E-Newsletter

July 2012

www.nva.org

This quarterly newsletter, which contains abstracts of articles published between March and June 2012, has been supported, in part, through a grant from the **Enterprise Holdings Foundation**

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

Feature Article

Deconstructing the neuropathic pain phenotype to reveal neural mechanisms.
von Hehn CA, Baron R, Woolf CJ
Neuron. 2012 Feb 23;73(4):638-52.

After nerve injury maladaptive changes can occur in injured sensory neurons and along the entire nociceptive pathway within the CNS, which may lead to spontaneous pain or pain hypersensitivity. The resulting neuropathic pain syndromes present as a complex combination of negative and positive symptoms, which vary enormously from individual to individual. This variation depends on a diversity of underlying pathophysiological changes resulting from the convergence of etiological, genotypic, and environmental factors. The pain phenotype can serve therefore, as a window on underlying pathophysiological neural mechanisms and as a guide for developing personalized pain medicine.

Vulvodynia / Chronic Vulvovaginal Pain

The recurrent pain and sexual sequelae of provoked vestibulodynia: a perpetuating cycle.
Basson R
J Sex Med. 2012 Jun 6. doi: 10.1111/j.1743-6109.2012.02803.x. [Epub ahead of print]

INTRODUCTION: Optimal management of provoked vestibulodynia (PVD), thought to be the most common form of chronic dyspareunia, is unclear. AIM: To integrate recent brain data on chronic pain circuitry with stress-induced neuroendocrine mechanisms in the skin and the stress burden (allostatic load) of women with PVD; to also clarify the typical chronicity and negative sexual sequelae associated with PVD; and then review modulation of pain circuitry by cognitive therapy and mindfulness practice and apply to PVD management. METHODS: Review of scientific publications in the areas of sexual medicine, pain, brain imaging, gynecology, stress response, mindfulness, and cognitive behavioral therapy (CBT). MAIN OUTCOME MEASURES: (i) A model of PVD to reflect its etiology, typical chronicity, and the detrimental effects on sexual function; (ii) Interventions of sexual rehabilitation based on principles underlying changes associated with CBT and mindfulness practice. RESULTS: A model emerges which reflects how stress-induced changes of pain amplification (central sensitization), characteristic of chronic pain conditions, may impair sexual response in addition to sexual dysfunction that arises from conscious pain avoidance and/or fear-related inattention to

sexual cues. Stress from low self-acceptance may be a major component of the allostatic load present in women with PVD, only to be exacerbated by the sexual dysfunction precipitated by the pain of intercourse. Mindfulness-based CBT appears promising to target both the pain and sexual suffering from PVD. CONCLUSION: New findings on brain activity associated with recurrent clinical pain, functional brain changes associated with CBT and mindfulness, plus new data on stress systems within the skin along with data on increased stress load in women with PVD, support the use of mindfulness-based CBT for the recurrent pain and sexual suffering from PVD.

Use of amitriptyline cream in the management of entry dyspareunia due to provoked vestibulodynia.
Pagano R, Wong S
J Low Genit Tract Dis. 2012 May 22. [Epub ahead of print]

OBJECTIVE: This study aimed to evaluate the effectiveness of topical amitriptyline 2% in sorbolene (cetomacrogol aqueous) cream in the management of patients with entry dyspareunia caused by provoked vestibulodynia. MATERIALS AND METHODS: A prospective study of 150 patients presenting with entry dyspareunia to a private gynecologist (R.P.) was undertaken during a 12-month period. Provoked vestibulodynia was diagnosed by the presence of pinpoint tenderness confined to the vulvar vestibule. Most patients (102) had purely provoked vestibulodynia, whereas 48 had both provoked and unprovoked pain. There were 7 patients with grade 1 dyspareunia (intercourse always painful but only occasionally preventing penetration), 83 patients with grade 2 (intercourse always painful preventing penetration on most occasions), and 60 patients with grade 3 (apareunic). Questionnaires were evaluated before and 3 months after commencement of treatment. No control group using placebo was studied because of the private-practice setting. RESULTS: Duration of symptoms varied from 1 to 30 years, the mean being 4.7 years. There was no response in 66 patients (44%). Of these, 16 patients ceased treatment early because of local skin irritation and hence were regarded as treatment failures. The 84 patients (56%) that responded were divided into 3 groups as follows: (i) 25 with a slight but noticeable improvement; (ii) 44 with a moderate degree of improvement; and (iii) 15 with an excellent response, describing intercourse as comfortable and pain free (10% of the total study group). Most patients in all 3 groups elected to continue application of the cream after completion of the study. The response rate was similar (48%) in the subgroup that also had unprovoked vestibulodynia. There was no difference in the response rate according to parity. The response rate was also similar in patients who had previously taken oral amitriptyline unsuccessfully. In these 44 patients, the overall response rate was 59%. CONCLUSIONS: Topical amitriptyline cream should be considered for first-line treatment in the management of patients with provoked vestibulodynia causing entry dyspareunia. The response rate is reasonable (56%), and it eliminates the problems with systemic administration, namely, drowsiness and the difficulty patients have in accepting antidepressant medication for their condition.

Rates of self-reported urinary, gastrointestinal, and pain comorbidities in women with vulvar lichen sclerosus.
Berger MB, Damico NJ, Menees SB, Fenner DE, Haefner HK
J Low Genit Tract Dis. 2012 May 22. [Epub ahead of print]

OBJECTIVE: The study aimed to determine the prevalences of comorbid disorders in women with vulvar lichen sclerosus. MATERIALS AND METHODS: A retrospective review of self-administered questionnaires regarding the health history of 308 women with lichen sclerosus seen at a vulvar clinic between 2006 and 2011 was performed. Responses to questions about urinary (overactive bladder [OAB], urinary incontinence [UI], and

stress UI), gastrointestinal (inflammatory bowel diseases, constipation, and irritable bowel syndrome), thyroid dysfunction and pain (interstitial cystitis, fibromyalgia, temporomandibular joint disorder, and vulvar pain) disorders were collected. The percentage of subjects self-reporting each comorbidity was compared with the published prevalence in the general population using a single-value binomial test. RESULTS: Subject demographics (data presented as median [range] or percentage): age, 56.4 years (20.0-92.5); body mass index, 27.5 kg/m (17.4-53.1); parity 2 (0-10); white, 92.9%; and biopsy proven 65.6%. Prevalences of self-reported comorbidities in our subjects are as follows: OAB, 15.3%; UI, 38.6%; stress UI, 27.9%; inflammatory bowel diseases, 1.9%; constipation, 32.5%; irritable bowel syndrome, 19.5%; thyroid dysfunction, 33.1%; interstitial cystitis, 2.6%; fibromyalgia, 9.1%; temporomandibular joint disorder, 13.0%; and vulvar pain, 83.1%. The prevalence of each disorder is significantly different from that in the general population, with all p values ≤ .02. CONCLUSIONS: Vulvar lichen sclerosus is associated with numerous bladder, bowel, and pain comorbidities. The prevalences of all of these disorders are higher in our subjects than the general population except OAB, which we find at approximately one third of the general population. Patients with lichen sclerosus should be screened for comorbidities that may affect their health and/or quality of life.

Long-term well-being after surgical or conservative treatment of severe vulvar vestibulitis.
Tommola P, Unkila-Kallio L, Paavonen J
Acta Obstet Gynecol Scand. 2012 May 23. doi: 10.1111/j.1600-0412.2012.01466.x. [Epub ahead of print]

OBJECTIVE: To compare long-term well-being of women who needed surgery or did not need surgery in the treatment of severe vulvar vestibulitis syndrome. We also attempted to identify factors explaining differences in the treatment response. DESIGN: An observational case-control study. SETTING: University Hospital vulva clinic. POPULATION: Sixty-six women diagnosed with severe vulvar vestibulitis and treated initially by conservative management during 1994-2005. Thirty-nine patients did not respond and underwent posterior vestibulectomy and 27 were managed without surgery. METHODS: Baseline patient characteristics, degree of dyspareunia, and details of management were collected from hospital charts. At the follow-up visit current dyspareunia, sexual well-being, somatic and mental health, and social support were analyzed. Vestibular tenderness was measured by swab-touch test. MAIN OUTCOME MEASURES: Visual analogue scale (VAS) for dyspareunia, sexual well-being, vestibular tenderness, and overall patient satisfaction at follow-up. RESULTS: Dyspareunia decreased significantly in both groups. VAS decreased 66.7% in the surgery group and 78.1% in the conservative treatment group, (p = 0.407). Posterior swab-touch test was negative more frequently after vestibulectomy. Long-term sexual well-being did not differ between the two groups. Overall, 89% of the patients in both groups were satisfied with the treatment. Patients with atopic skin problems were less likely to need surgery (odds ratio 0.2; 95% confidence interval 0.1-0.7). CONCLUSION: Patients with severe vulvar vestibulitis syndrome who do not respond to conservative management achieve good long-term well-being and decrease of dyspareunia by posterior vestibulectomy. The response is comparable to that achieved by conservative management among patients who do not need surgery.

Electromyography and vaginal pressure of the pelvic floor muscles in women with recurrent vulvovaginal candidiasis and vulvodynia.
Polpeta NC, Giraldo PC, Juliato CR, Yoshida LP, do Amaral RL, Eleutério J Jr
J Reprod Med. 2012 Mar-Apr;57(3-4):141-7.

OBJECTIVE: To evaluate the electrical potentials and pressure exerted by the pelvic floor muscles in women with recurrent vulvovaginal candidiasis (RVVC) or vulvodynia as compared to control women. STUDY DESIGN:

A cross-sectional study performed in the Female Outpatient Clinic of Genital Infections in the Department of Obstetrics and Gynecology of the Universidade Estadual de Campinas analyzed and compared electromyography (EMG) and vaginal pressure of the pelvic floor muscles in 61 women. Of these 61 women, 19 had vulvodynia, 12 had RVVC and 30 women had no disorder (control group). For data collection, the instrument used was the Miotool Uro device and its software Biotrainer (Miotec Ltd., Porto Alegre, Rio Grande do Sul, Brazil). RESULTS: The EMG evaluation of the pelvic floor muscles showed significantly lower values in the vulvodynia group (tonic contractions) and RVVC group (phasic and tonic contractions) when compared to the control group. No significant differences in basal tone EMG and vaginal pressure values at rest or during pelvic floor muscle contractions were found among groups. The maximum time of sustained contraction in patients with RVVC or vulvodynia was significantly lower ($p < 0.0001$) than in controls. CONCLUSION: Women with vulvodynia and RVVC have more frequent pelvic floor muscle dysfunction than controls when observed by EMG evaluation.

Comfort in discussing vulvar pain in social relationships among women with vulvodynia.
Nguyen RH, MacLehose RF, Veasley C, Turner RM, Harlow BL, Horvath KJ
J Reprod Med. 2012 Mar-Apr;57(3-4):109-14.

OBJECTIVE: To assess women's likelihood of feeling comfortable in discussing vulvar pain. STUDY DESIGN: Using a survey of women with self-reported clinician-diagnosed vulvodynia, we assessed the likelihood of comfort in discussing vulvar pain within four types of relationships: husband/partner, mother/sister, best friend, and other women friends. Separate multivariable models were fit for relationship type to determine whether vulvar pain characteristics (length, severity, family history) were associated with likelihood of feeling comfortable in discussing. RESULTS: A total of 67% of women with a partner were comfortable discussing their vulvar pain with that person, whereas 39% were comfortable with family and 26% were comfortable with women friends. Independent of age, the more years women had vulvodynia the less likely they would be comfortable discussing it. Compared to lower levels of vulvar pain, increasing levels (mild, moderate and severe) were associated with greater comfort in discussing their pain with friends; women were 10% more likely to be comfortable with each increase in pain level, and 12% more likely to be comfortable with other women friends. CONCLUSION: Our data suggest that vulvar pain characteristics may determine how comfortable a woman is to discuss her vulvar pain, but it varies by relationship type.

Assessment and management options for women with vulvodynia.
Cox KJ, Neville CE
J Midwifery Womens Health. 2012 May;57(3):231-40. doi: 10.1111/j.1542-2011.2012.00162.x.

Vulvodynia is a chronic pain disorder that affects sexual function in adult women. The etiology of vulvodynia is poorly understood, making the condition difficult to diagnose and treat. Women with vulvodynia often suffer significant psychological distress and have difficulty finding a compassionate and supportive health care provider. This article reviews the etiology, diagnosis, educational strategies, and treatment options for vulvodynia with the aim of increasing primary care providers' knowledge and assessment skills. Physical therapy and other nonsurgical treatment modalities are explored in depth.

Qualitative analysis of heterosexual women's experience of sexual pain and discomfort.
Sutherland O
J Sex Marital Ther. 2012 May;38(3):223-44.

In this qualitative analysis, the author explored heterosexual women's accounts of the lived experience of sexual pain and discomfort. The author's aim was to expand theoretical and empirical knowledge in the area of female sexual dysfunction by providing a detailed description of the subjective experience of female sexual concerns. The author used empirical phenomenological methodology to analyze the data generated during semi-structured in-depth interviews conducted with 9 women and generated 42 themes that were woven into a common story of the experience, its preconditions, coping strategies, and aftereffects. The limitations of the study and implications for research and clinical practice are discussed.

Characteristics of patients seeking outpatient rehabilitation for pelvic-floor dysfunction.
Wang YC, Hart DL, Mioduski JE
Phys Ther. 2012 Apr 26. [Epub ahead of print]

BACKGROUND: Pelvic floor dysfunction (PFD) affects a substantial proportion of individuals, especially women. OBJECTIVE: To describe the characteristics of individuals with disorders associated with PFD seeking outpatient physical therapy services and to identify the prevalence of specific pelvic floor disorders in the group. DESIGN: Prospective longitudinal cohort study of 2,452 patients (mean 50, SD 16, min 18, max 91 yrs) being treated in 109 outpatient physical therapy clinics in 26 states (USA) for their PFD. METHODS: We examined patient demographic variables and summarized patient self-reported responses to questions related to urinary and bowel functioning at admission prior to receiving the therapy for their PFD disorders. RESULTS: Patients were primarily female (92% female, 8% male), were under 65 years of age (39% 18 to <45 yrs; 39% 45 to <65 yrs; 21% 65 yrs or older), and had chronic symptoms (74% chronic). Overall, 67% of patients reported that they had urinary problems, 27% reported bowel problems, and 39% had pelvic pain. Among those who had urinary or bowel disorders, 32 and 54 percent reported leakage as their only problem. Among those who had pelvic pain, most patients reported that the pain was in the abdominal area (56%). Combinations of urinary, bowel, and/or pelvic floor pain disorders occurred in 31% of patients. LIMITATIONS: Since this study was a secondary analysis of prospectively collected data, the researchers were not in control of the data collection procedure. Missing data were common. CONCLUSIONS: Data suggested most patients with PFD receiving outpatient physical therapy services were female, younger than 65 years, and had disorders for more than 90 days. Combinations of urinary, bowel, and/or pelvic floor pain disorders were not uncommon.

Motor cortex stimulation in refractory pelvic and perineal pain: report of two successful cases.
Louppe JM, Nguyen JP, Robert R, Buffenoir K, de Chauvigny E, Riant T, Péréon Y, Labat JJ, Nizard J
Neurourol Urodyn. 2012 Jun 5. doi: 10.1002/nau.22269. [Epub ahead of print]

AIMS: In some patients, with refractory chronic pelvic and perineal pain, pain and quality of life are barely alleviated despite optimal medical treatment, infiltrations and surgical release of the pudendal nerve. The management of these patients is complex, especially after failure of neuromodulation techniques (spinal cord stimulation. S3 nerve root stimulation and direct stimulation of the pudendal nerve). We report the first two cases illustrating the value of motor cortex stimulation (MCS), in this new indication. METHODS: The history, decision-making process, intraoperative findings and results of this technique are presented. The perineal cortical area was identified by intraoperative motor evoked potentials in the external anal sphincter,

confirming its location in the primary motor cortex between the inferior and superior limb positions. As predictive value of repetitive transcranial magnetic stimulation (rTMS) in the identification of responders to MCS for pain is now established, we performed pre-operative rTMS sessions for both patients. RESULTS: The first patient was a 74-years-old woman who reported an 11-year history of left lateral perineal pain. The second patient was a 45-year-old woman who reported a 4-year history of perineal pain following hysterectomy with ovariectomy. After respectively 40 months and 19 months of follow up, both patients reported an improvement of pain ranging from 40 to 50%. Time to onset of pain on sitting was markedly improved from a few minutes to 90 minutes, and largely contributing to improvement of activities of daily living and of quality of life. CONCLUSION: These two first cases suggest that motor cortex stimulation constitutes a new treatment for refractory pelvic and perineal pain, and should be considered after failure of conventional neuromodulation techniques, especially spinal cord stimulation.

Successful treatment of pudendal neuralgia with tri-column spinal cord stimulation: case report.
Rigoard P, Delmotte A, Moles A, Hervochon R, Vrignaud T, Misbert L, Lafay N, D'houtaud S, Frasca D, Guenot C, Giot JP, Diallo B, Bataille B
Neurosurgery. 2012 May 30. [Epub ahead of print]

BACKGROUND AND IMPORTANCE: There is large variation in the success of decompressive surgery for pudendal neuralgia (PN), the most chronic, disabling form of perineal pain. We attempt to determine whether spinal cord stimulation (SCS) using new generation multi-column leads could form part of the treatment algorithm for refractory PN. CLINICAL PRESENTATION: A man with PN that was unresponsive to conventional treatment demonstrated a neuropathic component, and had a negative response to nerve infiltrations (so he was not indicated for decompressive surgery) and a positive response to perianal TENS, and was implanted with a 16-contacts surgical lead at the level of conus medullaris, allowing multi-column stimulation. Using transverse combinations, it was possible to obtain 100% paresthesia over the perineal area without unwanted dorsal root stimulation. Perineal and radicular pain was successfully relieved for up to 12 months (80% and 60% reduction in the visual analogue scores, respectively), with an improvement in all quality of life domains and a reduction in drug consumption. CONCLUSION: SCS using a 16-contacts lead may be a viable therapeutic option for patients with refractory PN who are contraindicated for decompressive surgery.

The hermunculus: what is known about the representation of the female body in the brain?
Di Noto PM, Newman L, Wall S, Einstein G
Cereb Cortex. 2012 Apr 17. [Epub ahead of print]

The representation of the body in the brain, the homunculus, was posited by Wilder Penfield based on his studies of patients with intractable epilepsy. While he mapped both male and female patients, Penfield reports little about the females. The now iconic illustration of the map is clearly male with testicles, penis, and no breasts. In order to bring attention to this omission and to stimulate studies of female somatosensory cortex (SS), we discuss what is known about the map of the female body in the brain, including Penfield's findings in his female patients and subsequent work by others exploring the human female SS. We reveal that there is much we do not know about how the entire female body is represented in the brain or how it might change with different reproductive life stages, hormones, and experiences. Understanding what is and is not currently known about the female SS is a first step toward fully understanding neurological and physiological sex differences, as well as producing better-informed treatments for pain conditions related to mastectomy,

hysterectomy, vulvodynia, and fibromyalgia. We suggest that the time is ripe for a full mapping of the female brain with the production of a hermunculus.

The somatic and autonomic innervation of the clitoris; preliminary evidence of sexual dysfunction after minimally invasive slings.
Bekker MD, Hogewoning CR, Wallner C, Elzevier HW, Deruiter MC
J Sex Med. 2012 Apr 10. doi: 10.1111/j.1743-6109.2012.02711.x. [Epub ahead of print]

INTRODUCTION: Vaginal sling procedures may have a negative effect on sexual function due to damage to vascular and/or neural genital structures. Even though autonomic innervation of the clitoris plays an important role in female sexual function, most studies on the neuroanatomy of the clitoris focus on the sensory function of the dorsal nerve of the clitoris (DNC). The autonomic and somatic pathways in relationship to sling surgery have up to the present not been described in detail. AIM: The aim of this study is to reinvestigate and describe the neuroanatomy of the clitoris, both somatic and autonomic, in relation to vaginal sling procedures for stress urinary incontinence. METHOD: Serially sectioned and histochemically stained pelves from 11 female fetuses (10-27 weeks of gestation) were studied, and three-dimensional reconstructions of the neuroanatomy of the clitoris were prepared. Fourteen adult female hemipelves were dissected, after a tension-free vaginal tape (TVT) (7) or tension-free vaginal tape-obturator (TVT-O) (7) procedure had been performed. MAIN OUTCOME MEASURES: Three-dimensional (3-D) reconstruction and measured distance between the clitoral nerve systems and TVT/TVT-O. RESULTS: The DNC originates from the pudendal nerve in the Alcock's canal and ascends to the clitoral bodies. In the dissected adult pelves, the distance of the TVT-O to the DNC had a mean of 9mm. The cavernous nerves originate from the vaginal nervous plexus and travel the 5 and 7 o'clock positions along the urethra. There, the autonomic nerves were found to be pierced by the TVT needle. At the hilum of the clitoral bodies, the branches of the cavernous nerves medially pass/cross the DNC and travel further alongside it. Just before hooking over the glans of the clitoris, they merge with DNC. CONCLUSION: The DNC is located inferior of the pubic ramus and was not disturbed during the placement of the TVT-O. However, the autonomic innervation of the vaginal wall was disrupted by the TVT procedure, which could lead to altered lubrication-swelling response.

Vulvodynia.
J Midwifery Womens Health. 2012 May;57(3):309-10. doi: 10.1111/j.1542-2011.2012.00173.x. Epub 2012 Apr 25.

No abstract available.

Assessment and management of vulval pain.
Nunns D, Murphy R
BMJ. 2012 Mar 28;344:e1723. doi: 10.1136/bmj.e1723.

No abstract available.

Magnetic resonance imaging-guided perineural therapy as a treatment option in young adults with pudendal nerve entrapment syndrome.
Schelhorn J, Habenicht U, Malessa R, Dannenberg C
Clin Neuroradiol. 2012 Apr 6. [Epub ahead of print]

No abstract available.

Chronic Pain

Managing chronic pain with nonopioid analgesics: a multidisciplinary consult.
Clauw D, McCarberg BH
Am J Med. 2012 May;125(5):S1.

As detailed in this online CME activity (www.cmeaccess.com/AJM/ChronicPain04), determining pain mechanism is an important aspect guiding treatment selection for chronic musculoskeletal pain states. Although broad classifications provide a framework, any combination of mechanisms may be present in a chronic pain patient, and there is growing evidence that pain states generally considered nociceptive may also involve elements of augmented central nervous system pain processing. Nonopioid analgesics, including serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and alpha-2-delta ligand anticonvulsants, are the treatments of choice for fibromyalgia and other central neuropathic pain states. Additionally, studies have now shown that certain SNRIs can be effective in treating "classic" nociceptive pain states, such as osteoarthritis, and also are effective for low back pain. In addition to considering biological mechanisms, chronic pain management also involves recognizing and evaluating the contribution of psychological and sociocultural factors that can influence pain chronicity and patient prognosis. A multimodal/multidisciplinary approach incorporating pharmacologic and nonpharmacologic therapy into a program that includes more than 1 discipline is important to improve outcomes in patients with chronic pain.

Comprehensive chronic pain management: improving physical and psychological function (CME multimedia activity).
McCarberg BH, Stanos S, Williams DA
Am J Med. 2012 Jun;125(6):S1.

As shown in this CME online activity (www.cmeaccess.com/AJM/ChronicPain02), chronic, non-cancer pain can arise from a variety of etiologies and can be broadly classified based on its underlying mechanism as nociceptive, inflammatory, neuropathic, or central, with some patients having pain arising from a combination of mechanisms. Chronic pain assessment and treatment involves evaluating not only its biological aspects, but also psychological and sociocultural factors. Beyond neural mechanisms, a patient's perception of chronic pain can be influenced by comorbid mood disorders, such as depression and anxiety; cognitive and affective traits, such as catastrophizing and fear-avoidance; environmental stressors, family relationships, social support, and cultural beliefs. Based on this biopsychosocial model, a multidisciplinary approach to management incorporates pharmacotherapy (opioid, nonopioid, and centrally-acting analgesics, and pain adjuvant medications) with nonpharmacologic physical rehabilitation and psychological and behavioral therapies to

address the multifactorial causes of chronic pain, which in turn leads to improvement of physical and psychological function.

Mechanisms-based assessment and treatment of pain: the art of fine dissection.
Siddall P
Pain. 2012 Jul;153(7):1348-9.

No abstract available.

Chronic pain: not only a matter of time.
Bonezzi C, Demartini L, Buonocore M
Minerva Anestesiol. 2012 Jun;78(6):704-11.

The term "chronic" is often used in daily clinical practice to indicate a type of pain that lasts over time and is accompanied by diagnostic and therapeutic difficulties. The common feeling is that in this category are actually collected many different clinical cases with the unique characteristic that the pain lasts a long time. It follows that treatment failures are common and patients roam from doctor to doctor in search of an effective care program. At the same time the health spending for the treatment of these patients is becoming increasingly high. In clinical practice we meet many patients with obscure pain syndromes which are classified as "chronic" and untreatable only because persist for long time and that obtain a complete pain relief after a right diagnosis and a specific treatment. In this review the Authors want to argue that the term chronic should not be used only when the pain persists for some time or just when signs and symptoms of mechanisms in the central nervous systems are present. The authors suggest that there is a clear difference between acute and chronic pain but also that in chronic pain patients there are three different painful conditions: 1) patients with a chronic disease (or sequelae) and with chronic pain in which the pain mechanisms are closely related to the underlying chronic disease (e.g., rheumatoid arthritis) or to previous injury that has generated other unsolvable mechanisms (e.g., deafferentation pain after plexus avulsion); 2) patients with a chronic disease and chronic pain in which new mechanisms overlap those related to the underlying disease; 3) patients with chronic pain in whom the correlation between pain and the initial tissue injury is lost and the persistence of pain is due to new developed mechanisms. According to this classification we can distinguish patients with "painful chronic disease" by patients with "independent chronic pain". In these latter cases the complexity of the clinical picture is to be found in a maladaptative response to pain, in emergence of central nervous system mechanisms and in behavioral changes that, in turn, can cause long-term social, psychological and physical sequelae. Differences among patients in developing chronic pain can be related to differences in the ability of the brain to continuously adapt its functional and structural organization. It is obvious that the care plan for these complex patients is profoundly different from that needed for patients with pain linked to a chronic disease or stabilized pain mechanisms. The purpose of the present article is to provide a review of the most noteworthy developments in this field and to propose some observations that may help to understand this pain condition and the patients.

Spinal mechanisms of pain and analgesia.
Miljanich G, Rauck R, Saulino M
Pain Pract. 2012 May 28. doi: 10.1111/j.1533-2500.2012.00564.x. [Epub ahead of print]

Chronic pain-especially that which is refractory to conventional treatment-presents particular challenges to physicians and patients. Examination of the molecular and cellular mechanisms involved in this pathophysiology suggests that spinal instillation of therapeutic agents may offer an effective treatment option through the modification of the processing and sensation of chronic pain. Intrathecal therapy, used alone or in combination with other analgesic agents, may reduce chronic pain by attenuating both pre- and postsynaptic activities. This article reviews chronic pain pathophysiology and the mechanisms whereby spinally administered analgesics may modify chronic pain. Available treatment options are also considered, including recommendations from the 2007 Polyanalgesic Consensus Conference (PACC) guidelines on the use of intrathecal agents for nociceptive, neuropathic, and mixed pain.

The influence of menstrual phases on pain modulation in healthy women.
Rezaii T, Hirschberg AL, Carlström K, Ernberg M
J Pain. 2012 May 25. [Epub ahead of print]

This study investigated if conditioned pain modulation (CPM) varies across the menstrual cycle in healthy, normally menstruating women and investigated correlations between sex hormone levels and CPM across the menstrual cycle. Thirty-six normally menstruating women were tested during 3 phases of the menstrual cycle: early follicular, ovulatory, and midluteal, confirmed by hormone determinations. Mechanical pressure (test stimulus) was applied to the masseter muscle and the induced pain assessed before, during, and after immersion of the hand into ice water (conditioning stimulus) to activate CPM or tepid water (control). Conditioning pain, ie, pain in the hand during CPM/control experiment, and tolerance time were also measured. Test pain intensity was suppressed during CPM in all phases ($P < .001$), but with more effective suppression during the ovulatry than during the early follicular phase ($P < .05$). There were no changes in test pain intensity during the control experiment and no significant differences in conditioning pain, or tolerance time between phases. In conclusion, our results showed more effective pain modulation in the ovulatory phase of the menstrual cycle, when estradiol levels are high and progesterone levels are low, than in the early follicular phase when both these hormones are low. PERSPECTIVE: Deficient pain modulation is believed to be an important pathogenic factor in many chronic pain conditions that affect women. This article shows that sex hormones modulate conditioned pain modulation, because pain inhibition was more effective in the ovulatory phase of the menstrual cycle than in the early follicular phase.

Progesterone produces antinociceptive and neuroprotective effects in rats with microinjected lysophosphatidic acid in the trigeminal nerve root.
Kim MJ, Shin HJ, Won KA, Yang KY, Ju JS, Park YY, Park JS, Bae YC, Ahn DK
Mol Pain. 2012 Mar 19;8:16. doi: 10.1186/1744-8069-8-16.

BACKGROUND: In our present study, we studied the role of demyelination of the trigeminal nerve root in the development of prolonged nociceptive behavior in the trigeminal territory. RESULTS: Under anesthesia, the Sprague-Dawley rats were mounted onto a stereotaxic frame and 3 μL of lysophosphatidic acid (LPA, 1 nmol) was injected into the trigeminal nerve root to produce demyelination. This treatment decreased the air-puff thresholds, persisted until postoperative day 130, and then returned to the preoperative levels 160 days after

LPA injection. The LPA-treated rats also showed a significant hyper-responsiveness to pin-prick stimulation. We further investigated the antinociceptive and neuroprotective effects of progesterone in rats undergoing demyelination of the trigeminal nerve root. Progesterone (8, 16 mg/kg/day) was administered subcutaneously, beginning on the operative day, for five consecutive days in the LPA-treated rats. Treatment with progesterone produced significant early anti-allodynic effects and delayed prolonged anti-allodynic effects. The expression of protein zero (P0) and peripheral myelin protein 22 (PMP22) were significantly down-regulated in the trigeminal nerve root on postoperative day 5 following LPA injection. This down-regulation of the P0 and PMP22 levels was blocked by progesterone treatment. CONCLUSIONS: These results suggest that progesterone produces antinociceptive effects through neuroprotective action in animals with LPA-induced trigeminal neuropathic pain. Moreover, progesterone has potential utility as a novel therapy for trigeminal neuropathic pain relief at an appropriate managed dose and is therefore a possible future treatment strategy for improving the recovery from injury.

Effect of milnacipran, a serotonin and noradrenaline reuptake inhibitor, on C-fiber-evoked field potentials in spinal long-term potentiation and neuropathic pain.
Ohnami S, Kato A, Ogawa K, Shinohara S, Ono H, Tanabe M
Br J Pharmacol. 2012 Apr 27. doi: 10.1111/j.1476-5381.2012.02007.x. [Epub ahead of print]

BACKGROUND AND PURPOSE: The analgesic action of serotonin and noradrenaline reuptake inhibitors (SNRIs) on nociceptive synaptic transmission in the spinal cord is poorly understood. We investigated the effects of milnacipran, an SNRI, on C-fiber-evoked field potentials (FPs) in spinal long-term potentiation (LTP), a proposed synaptic mechanism of hypersensitivity, and on the FPs in a neuropathic pain condition. EXPERIMENTAL APPROACH: C-fiber-evoked FPs by electrical stimulation of the sciatic nerve fibers were recorded in the spinal dorsal horn of anesthetized adult rats, and LTP was induced by high-frequency stimulation of the sciatic nerve fibers. A rat model of neuropathic pain was produced by L5 spinal nerve ligation and transection. KEY RESULTS: Milnacipran produced prolonged inhibition of C-fiber-evoked FPs when applied spinally after the establishment of LTP of C-fiber-evoked FPs in naïve animals. In the neuropathic pain model, spinal administration of milnacipran clearly reduced the basal C-fiber-evoked FPs. These inhibitory effects of milnacipran were blocked by spinal administration of methysergide, a 5-HT(1/2) receptor antagonist, and yohimbine or idazoxan, α(2) -adrenergic receptor antagonists. In contrast, the spinal administration of milnacipran in naïve animals did not affect the basal C-fiber-evoked FPs and the induction of spinal LTP. CONCLUSIONS AND IMPLICATIONS: Milnacipran inhibited C-fiber-mediated nociceptive synaptic transmission in the spinal dorsal horn after the establishment of spinal LTP and in the neuropathic pain model, by activating both spinal serotonergic and noradrenergic systems. The condition-dependent inhibition of the C-fiber-mediated transmission by milnacipran could provide novel evidence regarding the analgesic mechanism of SNRIs in chronic pain.

HCN2 ion channels: an emerging role as the pacemakers of pain.
Emery EC, Young GT, McNaughton PA
Trends Pharmacol Sci. 2012 May 19. [Epub ahead of print]

Acute nociceptive pain is caused by the direct action of a noxious stimulus on pain-sensitive nerve endings, whereas inflammatory pain (both acute and chronic) arises from the actions of a wide range of inflammatory mediators released following tissue injury. Neuropathic pain, which is triggered by nerve damage, is often considered to be very different in its origins, and is particularly difficult to treat effectively. Here we review

recent evidence showing that members of the hyperpolarization-activated cyclic nucleotide-modulated (HCN) ion channel family - better known for their role in the pacemaker potential of the heart - play important roles in both inflammatory and neuropathic pain. Deletion of the HCN2 isoform from nociceptive neurons abolishes heat-evoked inflammatory pain and all aspects of neuropathic pain, but acute pain sensation is unaffected. This work shows that inflammatory and neuropathic pain have much in common, and suggests that selective blockers of HCN2 may have value as analgesics in the treatment of pain.

Study of emotional and cognitive impairments in mononeuropathic rats: effect of duloxetine and gabapentin.
Grégoire S, Michaud V, Chapuy E, Eschalier A, Ardid D
Pain. 2012 Jun 2. [Epub ahead of print]

Chronic pain is a multidimensional experience that not only includes changes in nociception, but also impairments in emotion and cognitive functions. These last 2 components are not often taken into account in preclinical research. We investigated emotional and cognitive impairments in a model of neuropathic pain in rats induced by chronic constriction injury (CCI) of the sciatic nerve. Nociceptive response, anxiety and depressive-like behaviours as well as cognitive capacities were analysed, and the effect of per os administration of duloxetine and gabapentin was studied. In the electronic von Frey test, CCI rats exhibited mechanical hypersensitivity which can be influenced by duloxetine (3-30mg/kg) and gabapentin (10-30mg/kg). Cognitive impairments were found in the social but not in the spatial (Y-maze) recognition memory tests. Duloxetine and gabapentin dose-dependently (3-30mg/kg) restored social recognition memory impairment. Anxiety-like behaviour was only observed in the open-field test (decrease in the time spent in the inner zone) but not in the elevated plus maze or in the social interactions tests in CCI animals. In this test, impairment in locomotor activity (decrease of the total number of crossing) was also observed. Duloxetine and gabapentin (10mg/kg) were effective to increase the time spent in the inner zone as well as locomotor activity. No difference was observed in depressive-like behaviour (saccharin preference test) between sham-operated and CCI rats. These data suggest that cognitive rather than emotional impairments seem to be present in neuropathic CCI rats and can be reversed by duloxetine and gabapentin.

Effects of combined opioids on pain and mood in mammals.
Rech RH, Mokler DJ, Briggs SL
Pain Res Treat. 2012;2012:145965. Epub 2012 Mar 21.

The authors review the opioid literature for evidence of increased analgesia and reduced adverse side effects by combining mu-opioid-receptor (MOR) agonists, kappa-opioid-receptor (KOR) agonists, and nonselective low-dose-opioid antagonists (LD-Ant). We tested fentanyl (MOR agonist) and spiradoline (KOR agonist), singly and combined, against somatic and visceral pain models. Combined agonists induced additive analgesia in somatic pain and synergistic analgesia in visceral pain. Other investigators report similar effects and reduced tolerance and dependence with combined MOR agonist and KOR agonist. LD-Ant added to either a MOR agonist or KOR agonist markedly enhanced analgesia of either agonist. In accordance with other place-conditioning (PC) studies, our PC investigations showed fentanyl-induced place preference (CPP) and spiradoline-induced place aversion (CPA). We reduced fentanyl CPP with a low dose of spiradoline and reduced spiradoline CPA with a low dose of fentanyl. We propose combined MOR agonist, KOR agonist, and LD-Ant to produce superior analgesia with reduced adverse side effects, particularly for visceral pain.

CGRPα-expressing sensory neurons respond to stimuli that evoke sensations of pain and itch.
McCoy ES, Taylor-Blake B, Zylka MJ
PLoS One. 2012;7(5):e36355.

Calcitonin gene-related peptide (CGRPα, encoded by Calca) is a classic marker of nociceptive dorsal root ganglia (DRG) neurons. Despite years of research, it is unclear what stimuli these neurons detect in vitro or in vivo. To facilitate functional studies of these neurons, we genetically targeted an axonal tracer (farnesylated enhanced green fluorescent protein; GFP) and a LoxP-stopped cell ablation construct (human diphtheria toxin receptor; DTR) to the Calca locus. In culture, 10-50% (depending on ligand) of all CGRPα-GFP-positive (+) neurons responded to capsaicin, mustard oil, menthol, acidic pH, ATP, and pruritogens (histamine and chloroquine), suggesting a role for peptidergic neurons in detecting noxious stimuli and itch. In contrast, few (2.2±1.3%) CGRPα-GFP(+) neurons responded to the TRPM8-selective cooling agent icilin. In adult mice, CGRPα-GFP(+) cell bodies were located in the DRG, spinal cord (motor neurons and dorsal horn neurons), brain and thyroid-reproducibly marking all cell types known to express Calca. Half of all CGRPα-GFP(+) DRG neurons expressed TRPV1, ~25% expressed neurofilament-200, <10% contained nonpeptidergic markers (IB4 and Prostatic acid phosphatase) and almost none (<1%) expressed TRPM8. CGRPα-GFP(+) neurons innervated the dorsal spinal cord and innervated cutaneous and visceral tissues. This included nerve endings in the epidermis and on guard hairs. Our study provides direct evidence that CGRPα(+) DRG neurons respond to agonists that evoke pain and itch and constitute a sensory circuit that is largely distinct from nonpeptidergic circuits and TRPM8(+)/cool temperature circuits. In future studies, it should be possible to conditionally ablate CGRPα-expressing neurons to evaluate sensory and non-sensory functions for these neurons.

Current considerations for the treatment of severe chronic pain: the potential for tapentadol.
Pergolizzi J, Alegre C, Blake D, Alén JC, Caporali R, Casser HR, Correa-Illanes G, Fernandes P, Galilea E, Jany R, Jones A, Mejjad O, Morovic-Vergles J, Oteo Álvaro A, Radrigán Araya FJ, Simões ME, Uomo G
Pain Pract. 2012 Apr;12(4):290-306. doi: 10.1111/j.1533-2500.2011.00487.x.

Studies suggest that around 20% of adults in Europe experience chronic pain, which not only has a considerable impact on their quality of life but also imposes a substantial economic burden on society. More than one-third of these people feel that their pain is inadequately managed. A range of analgesic drugs is currently available, but recent guidelines recommend that NSAIDs and COX-2 inhibitors should be prescribed cautiously. Although the short-term efficacy of opioids is good, adverse events are common and doses are frequently limited by tolerability problems. There is a perceived need for improved pharmacological treatment options. Currently, many treatment decisions are based solely on pain intensity. However, chronic pain is multifactorial and this apaproach ignores the fact that different causative mechanisms may be involved. The presence of more than one causative mechanism means that chronic pain can seldom be controlled by a single agent. Therefore, combining drugs with different analgesic actions increases the probability of interrupting the pain signal, but is often associated with an increased risk of drug/drug interactions, low compliance and increased side effects. Tapentadol combines μ-opioid receptor agonism and noradrenaline reuptake inhibition in a single molecule, with both mechanisms contributing to its analgesic effects. Preclinical testing has shown that μ-opioid agonism is primarily responsible for analgesia in acute pain, whereas noradrenaline reuptake inhibition is more important in chronic pain. In clinical trials in patients with chronic pain, the efficacy of tapentadol was similar to that of oxycodone, but it produced significantly fewer gastrointestinal side-effects and treatment discontinuations. Pain relief remained stable throughout a 1-year safety study. Thus,

tapentadol could possibly overcome some of the limitations of currently available analgesics for the treatment of chronic pain.

Women, but not men, report increasingly more pain during repeated (un)predictable painful electrocutaneous stimulation: evidence for mediation by fear of pain.
Meulders A, Vansteenwegen D, Vlaeyen JW
Pain. 2012 Mar 6. [Epub ahead of print]

An abundance of animal research suggests that fear inhibits pain whereas anxiety increases it. Human studies on this topic are more scarce, and the existing evidence seems rather inconsistent. Therefore, we aimed to investigate the divergent effects of both negative emotional states-that is, pain-related fear and anxiety on pain sensitivity and unpleasantness. Possible sex-related differences were also under investigation, as well as the potential mediational role of fear of movement-related pain on the differences in pain intensity and unpleasantness between both sexes. We employed a voluntary joystick movement paradigm using movements as conditioned stimuli (CSs) and a painful electrocutaneous stimulus as the unconditioned stimulus. Healthy participants received predictable shocks in one condition and unpredictable shocks in another condition. The former procedure is known to induce fear of movement-related pain to the CS+ movement (movement consistently followed by pain), whereas the latter procedure induces (contextual) pain-related anxiety. Results showed that fear of movement-related pain indeed resulted in decreased pain intensity/unpleasantness ratings, while pain-related anxiety led to increased pain intensity/unpleasantness reports. Further, the anticipated sex difference was modulated by time. That is, women gradually reported more pain/unpleasantness, whereas men do not show such a sensitization effect. Moreover, this sex-specific sensitization is partially mediated by (conditioned) fear of movement-related pain. Women also report increasingly more fear of pain over conditioning blocks, while men do not. These results might be interesting in the light of the overrepresentation of women in a number of clinical pain conditions as well as anxiety disorders.

The distinction between "medically unexplained" and "medically explained" in the context of somatoform disorders.
Klaus K, Rief W, Brähler E, Martin A, Glaesmer H, Mewes R
Int J Behav Med. 2012 Jun 8. [Epub ahead of print]

PURPOSE: Medically unexplained symptoms (MUS) currently constitute the main diagnostic criterion of somatoform disorders. It has been proposed that the required dichotomization of somatic complaints into MUS and medically explained symptoms (MES) should be abandoned in DSM-V. The present study investigated complaints in the general population in order to evaluate the relevance of a distinction between MUS and MES. METHODS: Three hundred twenty-one participants from a population-based sample were interviewed by telephone to assess symptoms present during the previous 12 months. Complaints were examined in terms of health care use, diagnoses made by the physician and degree of impairment. At the 1-year follow-up, 244 subjects were re-interviewed in order to explore the stability of symptoms. RESULTS: The complaints frequently prompted participants to seek medical health care (several pain and pseudoneurological symptoms led to a doctors' visit in >80 % of cases), although etiological findings rarely suggested a medical pathology (occasionally <30 %). MUS and MES proved, to an equal degree, to impair individuals and prompt a change in lifestyle. Pain caused the worst impairment compared with other symptoms. The most prevalent MUS and MES were characterized by a transient course (approximately 60 %

remitted, 55 % newly emerged to follow-up), although various unexplained pain complaints tended to be persistent (e.g., back pain 67 %). Remarkably, the appraised etiology as explained or unexplained changed from baseline to follow-up in many persisting symptoms (20 % MUS → MES, 50 % MES → MUS). CONCLUSIONS: In principal, MUS and MES resulted in comparable impairment and stability. Due to conceptual and methodological difficulties, classification criteria for somatoform disorders should not be restricted to somatic aspects of the symptomatology.

Vulvovaginal Disorders

Identifying competencies in vulvar disorder management for medical students and residents: a survey of US vulvar disorder experts.
Venkatesan A, Farsani T, O'Sullivan P, Berger T
J Low Genit Tract Dis. 2012 May 30. [Epub ahead of print]

OBJECTIVE: The study aimed to perform a content validation process by surveying vulvar disorder experts to identify evidence-based competencies appropriate for use in developing vulvar curricula for medical trainees. MATERIALS AND METHODS: We identified 65 potential vulvar disorder competencies from literature review and expert opinions. Survey participants rated these competencies from 1 (not at all important) to 4 (highly important) in the training of 3 different groups of learners as follows: medical students, obstetrics and gynecology residents, and dermatology residents. We administered the survey to all US-based clinical members of the International Society for the Study of Vulvovaginal Disease as of September 2008 (n = 90). The content validity index and asymmetric CI were calculated for each curricular competency for each group of learners separately and used to identify competencies for use in curricula development. RESULTS: Forty-seven surveys were returned, yielding a response rate of 52.2%. Obstetrician-gynecologists represented 66% of the study sample, followed by dermatologists (15%), and nurse practitioners (9%). Seventy-nine percent of experts received their training by self-teaching, which included mentored experiences (62%) and attending conferences or courses (62%). Only 19% received vulvar training during residency and 11% during fellowship. Four curricular competencies met content validity criteria for medical students, 60 competencies for obstetrics and gynecology residents, and 47 competencies for dermatology residents. The differences between the 2 groups of residents focused on vulvovaginal pain and infection, examination, and procedures of the vagina. CONCLUSIONS: The competencies identified in this study can aid in the development of targeted curricula for medical students, obstetrics and gynecology residents, and dermatology residents.

Rates of self-reported urinary, gastrointestinal, and pain comorbidities in women with vulvar lichen sclerosus.
Berger MB, Damico NJ, Menees SB, Fenner DE, Haefner HK
J Low Genit Tract Dis. 2012 May 22. [Epub ahead of print]

OBJECTIVE: The study aimed to determine the prevalences of comorbid disorders in women with vulvar lichen sclerosus. MATERIALS AND METHODS: A retrospective review of self-administered questionnaires regarding the health history of 308 women with lichen sclerosus seen at a vulvar clinic between 2006 and 2011 was performed. Responses to questions about urinary (overactive bladder [OAB], urinary incontinence [UI], and stress UI), gastrointestinal (inflammatory bowel diseases, constipation, and irritable bowel syndrome), thyroid

dysfunction and pain (interstitial cystitis, fibromyalgia, temporomandibular joint disorder, and vulvar pain) disorders were collected. The percentage of subjects self-reporting each comorbidity was compared with the published prevalence in the general population using a single-value binomial test. RESULTS: Subject demographics (data presented as median [range] or percentage): age, 56.4 years (20.0-92.5); body mass index, 27.5 kg/m (17.4-53.1); parity 2 (0-10); white, 92.9%; and biopsy proven 65.6%. Prevalences of self-reported comorbidities in our subjects are as follows: OAB, 15.3%; UI, 38.6%; stress UI, 27.9%; inflammatory bowel diseases, 1.9%; constipation, 32.5%; irritable bowel syndrome, 19.5%; thyroid dysfunction, 33.1%; interstitial cystitis, 2.6%; fibromyalgia, 9.1%; temporomandibular joint disorder, 13.0%; and vulvar pain, 83.1%. The prevalence of each disorder is significantly different from that in the general population, with all p values ≤ .02. CONCLUSIONS: Vulvar lichen sclerosus is associated with numerous bladder, bowel, and pain comorbidities. The prevalences of all of these disorders are higher in our subjects than the general population except OAB, which we find at approximately one third of the general population. Patients with lichen sclerosus should be screened for comorbidities that may affect their health and/or quality of life.

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. [Epub ahead of print]

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.

Photodynamic therapy of vulvar lichen sclerosus et atrophicus in a woman with hypothyreosis - case report.
Osiecka BJ, Nockowski P, Jurczyszyn K, Ziólkowski P
Photodiagnosis Photodyn Ther. 2012 Jun;9(2):186-8.

Lichen sclerosus et atrophicus (LSA) is disease of skin and mucosa, its pathogenesis remains unknown. Itching, pain and burning sensations and atrophy of vulva impair quality of life. Treatment is symptomatic. We report case of 30-year old woman with lesions in vulva in which series of topical PDT were carried out. We applied Levulan(®)Kerastick(®) for 4h and after that lesions were illuminated with red light. Along with above treatment patient started receiving Euthyrox(®), because of recently diagnosed hypothyreosis. Significant relief from subjective symptoms was achieved and lesions in vulvar region disappeared. Combination of topical PDT with hormonal therapy allowed controlling course of disease and minimizing symptoms, and thus improved quality of life.

Recognition and management of vulvar dermatologic conditions: lichen sclerosus, lichen planus, and lichen simplex chronicus.
Thorstensen KA, Birenbaum DL
J Midwifery Womens Health. 2012 May;57(3):260-75. doi: 10.1111/j.1542-2011.2012.00175.x.

Lichen sclerosus, lichen planus, and lichen simplex chronicus are dermatologic conditions that can affect the vulva. Symptoms include vulvar itching, irritation, burning, and pain, which may be chronic or recurrent and can lead to significant physical discomfort and emotional distress that can affect mood and sexual relationships. With symptoms similar to common vaginal infections, women often seek care from gynecological providers and may be treated for vaginal infections without relief. Recognition and treatment of these vulvar conditions is important for symptom relief, sexual function, prevention of progressive vulvar scarring, and to provide surveillance for associated vulvar cancer. This article reviews these conditions including signs and symptoms, the process of evaluation, treatment, and follow-up, with attention to education and guidelines for vulvar care and hygiene.

Clinical, dermoscopic and histopathologic features of genital and extragenital lichen sclerosus.
Larre Borges A, Tiodorovic-Zivkovic D, Lallas A, Moscarella E, Gurgitano S, Capurro M, Apalla Z, Bruno J, Popovic D, Nicoletti S, Pérez J, Zalaudek I
J Eur Acad Dermatol Venereol. 2012 May 31. doi: 10.1111/j.1468-3083.2012.04595.x. [Epub ahead of print]

BACKGROUND: Little is currently known about the dermoscopic patterns of genital and extragenital lichen sclerosus (LS). In order to evaluate and compare the dermoscopic and histopathologic patterns of genital and extragenital lichen sclerosus, a retrospective analysis of clinical, dermoscopic and histopathologic features of genital and extragenital LS, collected between March 2010 and December 2011 at four dermatology clinics in Greece, Italy, Serbia and Uruguay was performed. OBSERVATIONS: A total of 29 lesions from 14 (mean age 62.8 years) and 12 (mean age 53.5 years) patients with genital and extragenital LS, respectively were analyzed. Mean duration of disease was 3.5 years for genital and 1.8 years for extragenital LS. White-yellowish structureless areas were seen in all cases of genital and extragenital LS; however linear vessels occurred at higher frequency in genital than in extragenital lesions (85.7% vs. 33.3%, respectively). Extragenital LS revealed two different time-related patterns: keratotic plugs were more prevalent in lesions with short duration (<2 years), whereas longer persisting lesions appeared atrophic and revealed fine chrysalis structures. CONCLUSIONS: Our morphologic study provides novel insights into the morphologic diversity of LS at different body sites and different stages of progression.

Coexistence of lichen sclerosus and morphea: a retrospective analysis of 472 patients with localized scleroderma from a German tertiary referral center.
Kreuter A, Wischnewski J, Terras S, Altmeyer P, Stücker M, Gambichler T
J Am Acad Dermatol. 2012 Apr 23. [Epub ahead of print]

BACKGROUND: The coexistence of lichen sclerosus (LiS) and localized scleroderma (LoS) has sporadically been reported in the literature. Recently, a prospective multicenter study demonstrated a surprisingly high percentage of genital LiS in patients with morphea. OBJECTIVE: The aim of this study was to determine the prevalence of LiS in a cohort of patients with LoS who presented at a tertiary referral medical center for connective tissue diseases in Germany. METHODS: We retrospectively evaluated the prevalence of genital and extragenital LiS in adult and pediatric patients with different subtypes of LoS. Secondary outcome measures

included demographic characteristics and prevalence of other concomitant autoimmune diseases. RESULTS: Of the 472 patients (381 adults, 91 children; mean age: 46 years; range, 4-88 years; female to male ratio: 3.5:1 in adults and 8:1 in children) with LoS, 27 (5.7%) also presented with LiS (19 extragenital and 8 genital lesions). LiS exclusively occurred in patients with plaque-type (morphea) and generalized LoS. Twenty-six of the 27 (96.2%) patients with concomitant LoS and LiS were adults. Compared with LiS in the general population, LiS was significantly more frequent in LoS as indicated by an odds ratio of 18.1 (95% confidence interval 2.6-134.2; P < .0001). In all, 38 (8.1%) patients with LoS had other autoimmune disorders (most frequently Hashimoto thyroiditis, rheumatoid arthritis, and alopecia areata). LIMITATIONS: This was a retrospective study. CONCLUSIONS: This large retrospective analysis confirms recent reports of a high prevalence of LiS in patients with LoS. Based on these findings, patients with LoS, especially those with morphea, should be carefully screened for concomitant LiS, including inspection of the anogenital region.

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.

Childhood lichen sclerosus is a rare but important diagnosis.
Jensen LS, Bygum A
Dan Med J. 2012 May;59(5):A4424.

INTRODUCTION: Lichen sclerosus (LS) is a chronic skin disorder with a predilection for the anogenital area. The disease is mostly seen in prepubertal and postmenopausal females. The lesions present as sharply demarcated white plaques encircling the vagina and anus. The atrophic form can lead to scarring of the affected area. MATERIAL AND METHODS: Retrospective analysis of hospital records of children (aged 1-18 years) seen at the Department of Dermatology and Allergy Centre in Odense from October 1998 to November 2010 with a definite clinical diagnosis of anogenital LS with/without a confirming biopsy. RESULTS: A total of 35 girls and one boy were diagnosed with anogenital LS. The diagnostic delay was 17 months. Pruritus, dysuria, bleeding

and constipation were the dominant complaints, while one patient was asymptomatic. Referral was made by general practitioners, private dermatologists and paediatricians. Sexual abuse was suspected in five cases. Ten patients underwent biopsy confirming LS. Before a definite diagnosis was given, many children were extensively treated with various topical and oral agents. In our outpatient clinic, 30 children were treated with potent/ultra-potent corticosteroids and five patients were treated with calcineurin inhibitors. CONCLUSION: General practitioners may overlook this disorder despite characteristic clinical features and effective symptomatic treatment. Diagnostic delay is a significant problem for both patient and family, and the lesions may mimic the findings of sexual abuse. Potent corticosteroids are very effective in symptomatic treatment.

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.

Lichen sclerosus in the oral mucosa: a rare form of presentation.
Louvain D, Moura Jacques C, Fernandes Ferreira A, Hoehl Carneiro L, Quintela L, Cuzzi T, Soares de Azevedo L, Moritz Trope B, Ramos-e-Silva M
Acta Dermatovenerol Croat. 2012;20(1):43-7.

Lichen sclerosus is a chronic inflammatory disease of unknown origin, which affects mostly women in the fifth and sixth decades of life, but can also occur in men and children. The involvement of the oral mucosa alone or together with other forms of presentation is extremely rare, requiring a differential diagnosis with other diseases of the oral cavity, particularly lichen planus. There are less than 30 cases of lichen sclerosus in the oral mucosa described in the literature and there are no reports on malignant transformation so far. We describe a patient with skin, oral and genital lesions of lichen sclerosus.

Systematic review and meta-analysis of randomized controlled trials on topical interventions for genital lichen sclerosus.
Chi CC, Kirtschig G, Baldo M, Lewis F, Wang SH, Wojnarowska F
J Am Acad Dermatol. 2012 Apr 5. [Epub ahead of print]

BACKGROUND: Lichen sclerosus (LS) is a chronic inflammatory dermatosis that occurs mainly in the anogenital area and causes itching and soreness. Progressive destructive scarring may result in burying of the clitoris in females and phimosis in males. Affected people have an increased risk of genital cancers. OBJECTIVE: We sought to assess the effects of topical interventions for genital LS. METHODS: We undertook a systematic

review and meta-analysis using the methodology of the Cochrane Collaboration. RESULTS: We included 7 randomized controlled trials with a total of 249 participants covering 6 treatments. Clobetasol propionate 0.05% was better than placebo in treating genital LS (participant-rated improvement/remission of symptoms: risk ratio 2.85 [95% confidence interval {CI} 1.45-5.61]; investigator-rated global degree of improvement: standardized mean difference [SMD] 5.74 [95% CI 4.26-7.23]) as was mometasone furoate 0.05% (change in clinical grade of phimosis: SMD -1.04 [95% CI -1.77 to -0.31]). We found no evidence supporting the efficacy of topical androgens and progesterone. There were no differences between pimecrolimus and clobetasol propionate in relieving symptoms through change in pruritus (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 in improving gross appearance (investigator-rated global degree of improvement: SMD -1.64 [95% CI -2.40 to -0.87]). LIMITATIONS: Most of the included studies were small. CONCLUSIONS: The current limited evidence supports the efficacy of clobetasol propionate, mometasone furoate, and pimecrolimus in treating genital LS. Further randomized controlled trials are needed.

Adjuvant clinical effects of polydeoxyribonucleotide in lichen sclerosus.
Laino L
Eur J Dermatol. 2012 Jun 1. [Epub ahead of print]

No abstract available.

Occlusion, urine and genital lichen sclerosus.
Bunker CB
Indian J Dermatol Venereol Leprol. 2012 May;78(3):367-8.

No abstract available.

Diagnostic usefulness of dermatoscopy in differentiating lichen sclerous et atrophicus from morphea.
Shim WH, Jwa SW, Song M, Kim HS, Ko HC, Kim MB, Kim BS
J Am Acad Dermatol. 2012 Apr;66(4):690-1.

No abstract available.

Cutaneous vulvar streptococcal infection.
Mirowski GW, Schlosser BJ, Stika CS
J Low Genit Tract Dis. 2012 Mar 28. [Epub ahead of print]

OBJECTIVE: This study aimed to determine the etiology of fine superficial fissures in women with vulvar pain. MATERIALS AND METHODS: The charts of women with vulvar complaints seen in the Mucosal Disorders Clinic at Northwestern University between April 2006 and May 2008 were reviewed. Outcome measures included mucocutaneous examination findings and results of microbiological swab cultures in the presence of fine, superficial, vulvar and/or perianal fissures. The presence of concomitant vulvar disorders was noted. RESULTS: Sixteen women who presented with vulvar pain were found to have fine, superficial, vulvar and/or perianal fissures with minimal or no erythema on examination. None had inflammatory vaginitis. Group B β-hemolytic

streptococcus (Streptococcus agalactiae) was recovered in 6 (37.5%) patients. All women with group B β-hemolytic streptococcus-positive cultures had a concomitant vulvar disorder; however, fissures were present despite appropriate treatment directed at the concomitant vulvar dermatosis. Three patients reported improvement in vulvar pain after treatment with antibiotics, and fissures had resolved by the time of follow-up examination in these 3 patients. CONCLUSIONS: Group B β-hemolytic streptococcus may cause painful fine superficial fissures and minimal erythema of vulvar skin. Obtaining microbiological cultures should be considered in the evaluation of vulvar pain even in the absence of purulent inflammatory vaginitis. The search for documentation and treatment of this relevant pathogen is a departure from published recommendations.

Biopsychosocial predictors of postmenopausal dyspareunia: the role of steroid hormones, vulvovaginal atrophy, cognitive-emotional factors, and dyadic adjustment.
Kao A, Binik YM, Amsel R, Funaro D, Leroux N, Khalifé S
J Sex Med. 2012 May 23. doi: 10.1111/j.1743-6109.2012.02771.x. [Epub ahead of print]

INTRODUCTION: Although dyspareunia experienced after menopause is widely attributed to declining estrogen levels and vulvovaginal atrophy, critical reviews of the literature have suggested that these factors are incomplete as explanatory mechanisms. Little is known about psychosocial factors that may also be implicated in postmenopausal dyspareunic pain. AIM: To determine the extent to which levels of estrogens and progesterone, vulvovaginal atrophy, cognitive-emotional factors, and dyadic adjustment are predictive of postmenopausal dyspareunic pain intensity. METHODS: A total of 182 postmenopausal dyspareunia sufferers underwent a structured interview concerning sociodemographic status as well as medical and pain histories, gynecological examination, cytological evaluation, a blood draw, and answered a series of self-report questionnaires. Given the large number of genital and pelvic pain variables measured, a principal components analysis was undertaken to identify a smaller number of components representing meaningful dimensions of genital and pelvic pain. MAIN OUTCOME MEASURES: Pain severity ratings during intercourse were obtained using the McGill Pain Questionnaire. Pain ratings were also obtained during gynecological assessment. Serum estrone, estradiol, and progesterone levels were measured via immunoassay. The Vaginal Atrophy Index and maturation value were used to determine vulvovaginal atrophy severity. Participants completed the Pain Catastrophizing Scale, State-Trait Anxiety Inventory, The Beck Depression Inventory-II, and Dyadic Adjustment Scale. RESULTS: Hormone levels were not found to be consistent predictors of pain severity. Maturation value and cognitive-emotional variables (e.g., catastrophization, depression, anxiety) were significant predictors of vestibular pain, which affected over 90% of our sample. Relationship adjustment variables were inversely associated with pain severity within several genital locations. CONCLUSIONS: Results suggest that the traditional hypoestrogen and vulvovaginal atrophy conceptualization of postmenopausal dyspareunia is an insufficient explanatory model, and that pain is also influenced by cognitive, affective, and dyadic factors.

Vulvar endometriosis presenting with dyspareunia: a case report.
Brug P, Gueye NA, Bachmann G
J Reprod Med. 2012 Mar-Apr;57(3-4):175-7.

BACKGROUND: Superficial dyspareunia can be caused by a multitude of medical and psychological conditions, including pathologic conditions of the vulva. Although infectious and inflammatory causes are more common, vulvar endometriosis is a rare and often overlooked etiology of dyspareunia. CASE: A 33-year-old woman, gravida 1, para 1, presented for a gynecologic consultation with a 2-year history of increasing dyspareunia and cyclical vulvar pain associated with a vulvar mass. Previous treatment with analgesics and sitz baths did not

alleviate the symptoms. Pelvic examination revealed a right Bartholin's gland mass that was tender to palpation. The working diagnosis was a Bartholin's cyst as the cause of the dyspareunia, and the patient was scheduled for marsupialization and/or resection. Examination under anesthesia revealed an irregular, 5 cm, solid mass that extended into the labia majora, which was excised. Pathologic examination of the mass revealed endometriosis. The postoperative course was unremarkable and the patient reported complete resolution of symptoms. CONCLUSION: This case illustrates that superficial dyspareunia associated with cyclical vulvar pain can be caused by endometriosis involving the labia majora.

Vulvar skin atrophy induced by topical glucocorticoids.
Johnson E, Groben P, Eanes A, Iyer P, Ugoeke J, Zolnoun D
J Midwifery Womens Health. 2012 May;57(3):296-9. doi: 10.1111/j.1542-2011.2012.00189.x.

Steroid-induced skin atrophy is the most frequent and perhaps most important cutaneous side effect of topical glucocorticoid therapy. To date, it has not been described in vulvar skin. A patient presented with significant vulvar skin atrophy following prolonged steroid application to treat vulvar dermatitis. The extensive atrophy in the perineum resulted in secondary "webbing" and partial obstruction of the genital hiatus and superimposed dyspareunia. Prolonged use of topical steroids may result in atrophic changes in vulvar skin. Further research in clinical correlates of steroid-induced atrophy in the vulvar region is warranted.

Evaluation of vulvovaginal symptoms and Candida colonization in women with type 2 diabetes mellitus treated with canagliflozin, a sodium glucose co-transporter 2 inhibitor.
Nyirjesy P, Zhao Y, Ways K, Usiskin K
Curr Med Res Opin. 2012 May 25. [Epub ahead of print]

BACKGROUND/OBJECTIVE: Women with type 2 diabetes mellitus (T2DM) are at increased risk for vaginal Candida colonization, perhaps because of glucosuria. Sodium glucose co-transporter 2 (SGLT2) inhibitors in development for treatment of T2DM, improve glycemic control by increasing urinary glucose excretion. Vaginal Candida colonization and symptomatic vulvovaginal adverse events (VVAE) were assessed in females with T2DM treated with canagliflozin, a SGLT2 inhibitor. METHODS: In a double-blind study, subjects with T2DM and inadequate glycemic control on metformin were randomized to placebo; canagliflozin 50, 100, 200, 300 mg daily or 300 mg twice daily; or sitagliptin 100 mg daily for 12 weeks. Vaginal swabs for Candida culture were collected from 198 female subjects at baseline and week 12, and during the trial if symptoms consistent with vulvovaginal candidiasis occurred. RESULTS: At baseline, 23/198 (12%) females had vaginal cultures positive for Candida (C. glabrata: 14; C. albicans: 5; other: 4), with age ≤55 years associated with increased risk (overall risk [OR] 3.5; 95% confidence interval [CI], 1.1-10.7). Of those with negative cultures at baseline, 31% of canagliflozin and 14% of placebo/sitagliptin subjects converted to positive at week 12 (OR 2.8, 95% CI, 1.0-7.3 for canagliflozin vs. placebo/sitagliptin). Two placebo/sitagliptin (3%) and 16 canagliflozin subjects (10%) experienced VVAE. Positive vaginal culture for Candida species at baseline was a risk factor for VVAE (OR 9.1; 95% CI: 2.4-34.0). All 9/9 subjects in the canagliflozin group with a vaginal culture taken at the time of the VVAE were positive for Candida species. Most VVAE were treated with antifungal therapy and resolved without study drug interruption; none led to discontinuation. Study limitations include small population, short duration, and not obtaining cultures in all women with VVAE. CONCLUSION: Canagliflozin treatment was associated with an increase in vaginal colonization with Candida species and in VVAE in women with T2DM.

The in vitro antimicrobial activities of metabolites from lactobacillus strains on Candida species implicated in Candida vaginitis.

Ogunshe AA, Omotoso MA, Bello VB

Malays J Med Sci. 2011 Oct;18(4):13-25.

BACKGROUND: Research from developing countries, such as Nigeria, on Lactobacillus species in the female urogenital tract and their role as a barrier to vaginal infection is limited. Therefore, the aim of this study was to assess the clinical biotherapeutic potential of indigenous Lactobacillus species. METHODS: Antimicrobial metabolites production were characterised using simple and easily reproducible qualitative and quantitative methods. The in vitro inhibitory effect of Lactobacillus antimicrobials on vulvovaginal candidiasis-associated Candida species was investigated using modified agar spot and agar well-diffusion methods. RESULTS: The maximum levels of lactic acid, hydrogen peroxide, and diacetyl from 20 vaginal Lactobacillus strains from diseased subjects were 1.46 mg/L, 1.36 mmol/L, and 1.72 mg/L respectively. From the 4 healthy subjects, the maximum level of lactic acid was 1.08 mg/L; hydrogen peroxide, 1.36 mmol/L; and diacetyl, 0.86 mg/L. The maximum productions of these substances occurred between 72 and 120 hours of incubation. The in vitro antagonistic activities of vaginal L. acidophilus, L. fermentum, L. brevis, L. plantarum, L. casei, L. delbrueckii, and L. jensenii from diseased subjects inhibited a maximum of 5.71% of the 35 Candida species tested, while vaginal L. acidophilus and L. plantarum from healthy subjects inhibited between 57.1% and 68.6% of Candida species in vitro. CONCLUSION: Antimicrobial-producing lactobacilli can be considered as adjunct biotherapeutic candidates for the treatment of vulvovaginal candidiasis.

Short-course treatment of vulvovaginal candidiasis: comparative study of fluconazole and intra-vaginal fenticonazole.

Murina F, Graziottin A, Felice R, Di Francesco S, Mantegazza V

Minerva Ginecol. 2012 Apr;64(2):89-94.

AIM: The aim of this paper was to compare the efficacy of fluconazole 150 mg and intra-vaginal fenticonazole 600mg in short-course treatment of the acute episode of vulvovaginal candidiasis (VVC). METHODS: In a prospective study, 80 patients with clinical and mycological (SavvyCheck™ test) confirmed VVC were enrolled and divided randomly in two groups. Forty patients received oral fluconazole (150 mg), whereas 40 patients received intra-vaginal tablet fenticonazole (600 mg). Two sequential doses of azole agents were given 3 days apart (short-course treatment). Second and third visits were done for all patients seven and 30±5 days after treatment. RESULTS: At the second visit, 31 patients (77.5%) were cured clinically (Sobel score <4) in fluconazole group and 32 patients (80%) in fenticonazole group (P=0.876). The vulvovaginal pruritus was reduced in lower time in fenticonazole patients than in fluconazole group (mean 2.3 days versus 4.5 days, P=0.047). At the third visit, three patients in fluconazole group and two patients in fenticonazole group had clinical sign of VVC. CONCLUSION: Fluconazole and intravaginal fenticonazole are both effective to cure symptoms of VVC but fenticonazole appears to reduce the pruritus in less time.

Use of complementary and alternative medicine in recurrent vulvovaginal candidiasis-Results of a practitioner survey.

Watson CJ, Pirotta M, Myers P

Complement Ther Med. 2012 Aug;20(4):218-21. Epub 2012 Feb 22.

BACKGROUND: The mainstream long term management of recurrent vulvovaginal candidiasis (RVVC) often results in poor outcomes. It is expensive and unacceptable for many women who therefore have incorporated complementary and alternative medicine (CAM) into their personal care plan. OBJECTIVE: To ascertain clinicians' knowledge of CAM and their recommendations for the use of CAM and non-pharmacological management in women with RVVC. DESIGN AND SETTING: Anonymous, single page, self completed survey using convenience sampling at a vulval disorders meeting in New South Wales, Australia in 2009. PARTICIPANTS: Sixty six health professionals (medical practitioners, dermatologists, nurses and allied health professionals). RESULTS: Most clinicians reported asking about their patients' use of CAM and non-pharmacological management of RVVC, although only around half reported recommending it. CAM management included lactobacillus, oral and vaginal yoghurt, vinegar, garlic, Chinese medicine and tea-tree oil. Non-pharmacological management included dietary changes and use of cotton undergarments. Lactobacillus was the most commonly recommended CAM. CONCLUSION: CAM is popular with patients and many clinicians actively recommend its use in RVVC despite limited supporting evidence. Further research in the area of CAM and RVVC is long overdue.

Guideline vulvovaginal candidosis (2010) of the German Society for Gynecology and Obstetrics, the Working Group for Infections and Infectimmunology in Gynecology and Obstetrics, the German Society of Dermatology, the Board of German Dermatologists and the German Speaking Mycological Society.

Mendling W, Brasch J

Mycoses. 2012 Jul;55 Suppl 3:1-13. doi: 10.1111/j.1439-0507.2012.02185.x.

Candida (C.) species colonize the estrogenized vagina in at least 20% of all women. This statistic rises to 30% in late pregnancy and in immunosuppressed patients. The most often occurring species is Candida albicans. Host factors, especially local defense deficiencies, gene polymorphisms, allergic factors, serum glucose levels, antibiotics, psychosocial stress and estrogens influence the risk for a Candida vulvovaginitis. In less than 10% of all cases, non-albicans species, especially C. glabrata, but in rare cases also Saccharomyces cerevisiae, cause a vulvovaginitis, often with fewer clinical signs and symptoms. Typical symptoms include premenstrual itching, burning, redness and non-odorous discharge. Although pruritus and inflammation of the vaginal introitus are typical symptoms, only less than 50% of women with genital pruritus suffer from a Candida vulvovaginitis. Diagnostic tools are anamnesis, evaluation of clinical signs, the microscopic investigation of the vaginal fluid by phase contrast (400 x), vaginal pH-value and, in clinically and microscopically uncertain or in recurrent cases, yeast culture with species determination. The success rate for treatment of acute vaginal candidosis is approximately 80%. Vaginal preparations containing polyenes, imidazoles and ciclopiroxolamine or oral triazoles, which are not allowed during pregnancy, are all equally effective. C. glabrata is resistant to the usual dosages of all local antimycotics. Therefore, vaginal boric acid suppositories or vaginal flucytosine are recommended, but not allowed or available in all countries. Therefore, high doses of 800 mg fluconazole/day for 2-3 weeks are recommended in Germany. Due to increasing resistence, oral posaconazole 2 × 400 mg/day plus local ciclopiroxolamine or nystatin for 15 days was discussed. C. krusei is resistant to triazoles. Side effects, toxicity, embryotoxicity and allergy are not clinically important. A vaginal clotrimazole treatment in the first trimester of pregnancy has shown to reduce the rate of preterm births in two studies. Resistance of C. albicans does not play a clinically important role in vulvovaginal candidosis. Although it is not necessary to

treat vaginal candida colonization in healthy women, it is recommended in the third trimester of pregnancy in Germany, because the rate of oral thrush and diaper dermatitis in mature healthy newborns, induced by the colonization during vaginal delivery, is significantly reduced through prophylaxis. Chronic recurrent vulvovaginal candidosis requires a "chronic recurrent" suppression therapy, until immunological treatment becomes available. Weekly to monthly oral fluconazole regimes suppress relapses well, but cessation of therapy after 6 or 12 months leads to relapses in 50% of cases. Decreasing-dose maintenance regime of 200 mg fluconazole from an initial 3 times a week to once monthly (Donders 2008) leads to more acceptable results. Future studies should include candida autovaccination, antibodies against candida virulence factors and other immunological trials. Probiotics should also be considered in further studies. Over the counter (OTC) treatment must be reduced.

Microsatellite analysis of Candida isolates from recurrent vulvovaginal candidiasis.
Amouri I, Sellami H, Abbes S, Hadrich I, Mahfoudh N, Makni H, Ayadi A
J Med Microbiol. 2012 Apr 26. [Epub ahead of print]

C. albicans and C. glabrata were the most common causative agent of both VVC and RVVC. Studying the population structure and genotype differentiation of Candida species that cause RVVC may lead to a significant clinical management. A total of 106 isolates were collected from 55 patients subdivided into three groups. Group I regrouped 15 patients with RVVC (n= 50 isolates); group II recovered 16 patients from which two isolates were obtained and whose had at least a history of 2 episodes of VVC in last year (n= 32). Group III comprised 24 patients (n= 24) who had a single episode of VVC in 1-year period. C. albicans microsatellite markers CAI, CAIII and CAIV and C. glabrata RPM2, MTI and ERG3 microsatellites were amplified in a multiplex PCR. All isolates were subjected to genetic population analysis. Population genetic analysis provided evidence that there is a predominantly clonal population structure of C. albicans in each group. However, recombination was detected to some degree in C. albicans isolates in group III. There is a genetic homogeneity between the different C. albicans groups. Though, C. glabrata isolates showed an important genetic differentiation between group I and group III (FST= 0.207). Genotype analysis revealed that C. glabrata and C. albicans strains dominant genotypes were more prevalent in patients with RVVC. The frequent scenario for recurrences in our study was the strain replacement (53.3%). In conclusion, the identification of recurrence associated genotypes and specific C. glabrata population structure in RVVC group could be a significant marker in further investigations in virulence factors and RVVC management.

A novel approach to the surgical management of clitoral phimosis.
Kroft J, Shier M
J Obstet Gynaecol Can. 2012 May;34(5):465-71.

BACKGROUND: The objective of this case series was to outline a novel method for surgical correction of clitoral phimosis caused by vulvar lichen sclerosus (LS) or lichen planus (LP) and to review the postoperative outcomes. CASE SERIES: We used the CO2 laser to treat clitoral phimosis in 20 women with LS and three women with LP. All patients underwent individualized preoperative and postoperative topical therapy with steroids or immunomodulators. Five women with LS had mild reagglutination during follow-up but were satisfied with the results, and three required reoperation, with satisfactory results in follow-up. Two women with LP required reoperation. CONCLUSION: This novel surgical technique has enabled the treatment of clitoral phimosis secondary to LS or LP, but further studies are required. Medical maintenance therapy postoperatively is a vital component of treatment.

Incapacitating pelvic congestion syndrome in a patient with a history of May-Thurner Syndrome and left ovarian vein embolization.

Rastogi N, Kabutey NK, Kim D

Ann Vasc Surg. 2012 Jul;26(5):732.e7-732.e11.

BACKGROUND: The aim of this article is to report a rare case of unresolved incapacitating pelvic congestion syndrome (PCS) in a patient with a history of May-Thurner syndrome previously treated with stenting and left ovarian vein embolization. Additionally, this article highlights the role of pelvic venography in patients with PCS and reviews the coexistence. METHODS: A 32-year-old woman was referred to us for the evaluation of recurrent pelvic pain and dyspareunia requiring analgesics. Initially, she developed left lower-extremity deep vein thrombosis a few months after her first pregnancy. On further workup, she was diagnosed with May-Thurner syndrome and underwent left common iliac and left external iliac vein stenting. Furthermore, left ovarian vein coil embolization was performed for symptoms suggesting PCS at the same outside facility. The patient was referred to us for persistent pelvic pain approximately 1 year after she underwent left ovarian vein coil embolization. A diagnosis of incompletely resolved PCS was considered. RESULTS: Iliocaval venogram demonstrated patent left common iliac and external iliac venous stents in situ. Subsequent right ovarian venogram revealed a patent, but grossly dilated, right ovarian vein with retrograde flow and cross-pelvic collaterals confirming grade III PCS. Right ovarian vein coil embolization was performed, with excellent patient outcome. CONCLUSION: In the setting of a combined diagnosis of PCS and May-Thurner syndrome, persistent incapacitating PCS after initial iliac stenting should be followed with a complete pelvic venous evaluation including ovarian and left renal venography to rule out residual pelvic congestion secondary to any coexisting ovarian vein incompetencies or nutcracker syndrome.

Women's poorer satisfaction with their sex lives following gynecologic cancer treatment.

Lara LA, de Andrade JM, Consolo FD, Romão AP

Clin J Oncol Nurs. 2012 Jun 1;16(3):273-7.

Gynecologic cancer treatment can lead to anatomical changes in the genitalia that may impair sexual response. As a result, the authors aimed to assess women's self-perceptions of their sex lives following gynecologic cancer treatment and the impact of such treatment on sexual function. Thirty sexually active women were examined. At the first meeting with a physician sex therapist, women were asked about their satisfaction with their sexual activities prior to and after gynecologic cancer treatment, either with a partner or alone, and how many times per month they had sexual intercourse prior to the cancer diagnosis and after treatment. Women reported significantly worse sex lives and a significantly lower frequency of sexual relations following cancer treatment. All participants reported pain on vaginal penetration and feeling uncomfortable in discussing their sexual difficulties with the oncologist. The findings show that women experienced impaired sexual function, as well as poorer quality of sexual function, following gynecologic cancer treatment. Nurses should provide basic guidelines about sexual function to all patients who undergo treatment for gynecologic cancer.

The use of hormone therapy for the maintenance of urogynecological and sexual health post WHI.

Nappi RE, Davis SR

Climacteric. 2012 Jun;15(3):267-74.

BACKGROUND: The loss of estrogen at menopause and the gradual decline in testosterone with age are associated with urogenital atrophy and, as a result, urogenital tract symptoms, including lower urinary tract symptoms and dyspareunia. These symptoms will persist unless treated. OBJECTIVE: To review the prevalence of urogenital tract symptoms and sexual health problems associated with menopause and the role in the use of hormone therapy for the treatment of symptomatic women, with a specific focus on what has been learned since the first publication of the Women's Health Initiative (WHI) estrogen and estrogen + progestin studies. CONCLUSION: Studies support the use of local estrogen therapy, but not systemic estrogen therapy, for the treatment of urge urinary incontinence, overactive bladder and to reduce the number of urinary tract infections. The current evidence does not favor a beneficial effect on stress urinary incontinence. Local estrogen therapy is effective for the treatment of dyspareunia caused by vulvovaginal atrophy. Preliminary studies suggest a potential role for both intravaginal dehydroepiandrosterone and testosterone in the treatment of dyspareunia secondary to vulvovaginal atrophy, however, confirmatory studies are required before either therapy can be recommended. Post WHI, there is a need for medical practitioners to proactively raise the topic of urogynecological and sexual health in order to discuss the most suitable treatment option.