NVA Research Update E-Newsletter

October 2013
www.nva.org

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

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

Feature Article

Lessons in pain relief--a personal postgraduate experience.
Pizzo PA
N Engl J Med. 2013 Sep 19;369(12):1092-3. doi: 10.1056/NEJMp1306467.
www.ncbi.nlm.nih.gov/pubmed/24047058

"When I chaired an Institute of Medicine (IOM) committee on 'Relieving Pain in America' and then coauthored a Perspective article about the vast human toll and financial burden imposed by chronic pain, I believed I understood the impact of chronic pain. Not only did I have experience caring for children with life-threatening and frequently painful disorders, I also had relatives with chronic pain syndromes and had witnessed the limitations of the medical care system. But it wasn't until my own year-long journey with chronic pain that I received a higher-level education on the topic…"

Vulvodynia / Vulvovaginal Pain

Prevalence of symptoms consistent with a diagnosis of vulvodynia: Population-based estimates from two geographical regions.
Harlow BL, Kunitz CG, Nguyen RH, Rydell SA, Turner RM, Maclehose RF
Am J Obstet Gynecol. 2013 Sep 27. pii: S0002-9378(13)00987-3. doi: 10.1016/j.ajog.2013.09.033. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24080300

OBJECTIVES: We used validated sensitive and specific questions associated with clinically-confirmed diagnoses of unexplained vulvar pain (Vulvodynia) to compare the cumulative incidence of vulvar pain and prevalence of care seeking behavior in Boston, Massachusetts metropolitan area (BMA) and in Minneapolis/St. Paul (MSP), Minnesota, between 2001-2005 using census-based data, and 2010-2012, using outpatient community-clinic data, respectively. STUDY DESIGN: We received self-administered questionnaires from 5,440 women in BMA and 13,681 in MSP, 18-40 years of age, describing their history of vulvar burning or pain on contact that persisted >3 months that limited/prevented intercourse. RESULTS: By age 40, 7-8% in BMA and MSP reported vulvar pain consistent with Vulvodynia. Women of Hispanic/Latina origin compared to Caucasians were 1.4 times more likely to develop vulvar pain symptoms (95%CI: 1.1-1.8). Many women in MSP (48%) and BMA (30%) never sought treatment, and >50% who sought care with known health care access received no diagnosis. CONCLUSIONS: Using identical screening methods, we report high prevalence of vulvar pain in two geographical regions, and that access to health care does not increase the likelihood of seeking care for chronic vulvar pain.

Oral contraceptive use and risk of vulvodynia: a population-based longitudinal study.
Reed B, Harlow S, Legocki L, Helmuth M, Haefner H, Gillespie B, Sen A
BJOG. 2013 Aug 13. doi: 10.1111/1471-0528.12407. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23937077

OBJECTIVE: To assess whether the risk of vulvodynia is associated with previous use of oral contraceptives (OCs). DESIGN: Longitudinal population-based study. SETTING: Four counties in south-east Michigan, USA. POPULATION: A population-based sample of women aged 18 years and older, enrolled using random-digit dialing. METHODS: Enrolled women completed surveys that included information on demographic characteristics, health status, current symptoms, past and present OC use, and a validated screen for vulvodynia. The temporal relationship between OC use and subsequent symptoms of vulvodynia was assessed using Cox regression, with OC exposure modeled as a time-varying covariate. MAIN OUTCOME MEASURE: Vulvodynia, as determined by validated screen. RESULTS: Women aged <50 years who provided data on OC use, completed all questions required for the vulvodynia screen, and had first sexual intercourse prior to the onset of vulvodynia symptoms were eligible (n = 906). Of these, 71.2% (n = 645) had used OCs. The vulvodynia screen was positive in 8.2% (n = 74) for current vulvodynia and in 20.8% (n = 188) for past vulvodynia. Although crude cross-tabulation suggested that women with current or past vulvodynia were less likely to have been exposed to OCs prior to the onset of pain (60.7%), compared with those without this disorder (69.3%), the Cox regression analysis identified no association between vulvodynia and previous OC use (HR 1.08, 95% CI 0.81-1.43, P = 0.60). This null finding persisted after controlling for ethnicity, marital status, educational level, duration of use, and age at first OC use. CONCLUSION: For women aged <50 years of age, OC use did not increase the risk of subsequent vulvodynia.

Attributes and barriers to care of pelvic pain in university women.
Mann J, Shuster J, Moawad N
J Minim Invasive Gynecol. 2013 Aug 24. pii: S1553-4650(13)00278-1. doi: 10.1016/j.jmig.2013.05.003. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23981982

STUDY OBJECTIVE: To describe rates of pelvic pain in university women ages 18 and older and to explore the barriers to adequate health care for pelvic pain in this population. DESIGN: A cross-sectional study (Canadian Task Force classification II-2). SETTING: University of Florida, Gainesville, FL. PATIENTS: A total of 2000 female students at the University of Florida were randomly selected for participation. INTERVENTIONS: The 2000 sample members were sent a questionnaire to be completed online. MEASUREMENTS AND MAIN RESULTS: The online questionnaire was hosted through the REDCap electronic data capture tool hosted at the University of Florida. This questionnaire included demographic items, general health and health behavior questions, measures to assess different types of pelvic pain (e.g., dysmenorrheal; dyspareunia; urinary, bowel, and vulvar pain), items regarding barriers to care for pelvic pain problems, and quality of life measures. Data were exported to SAS software (SAS Institute Inc., Cary, NC) for analysis. Of the 2000 subjects who received the questionnaire invitation, 390 filled out the questionnaire, yielding a response rate of 19.5%. Respondents' ages ranged from 18 to 62 with a mean of 23 years. A total of 72.8% of respondents reported experiencing pelvic pain over the past 12 months. Dysmenorrhea was reported by nearly 80% of participants, over one third of participants noted deep dyspareunia, and a significant proportion of participants reported symptoms related to bowel movements. Vulvar symptoms, including superficial dyspareunia, were reported by 21.5% of participants. Most participants with pelvic pain (78.8%) have not received any diagnosis for their pain, whereas 73.6% reported not yet having visited a doctor. Significant barriers to receiving adequate medical care were reported, including difficulty with insurance coverage and physicians' lack of time and knowledge or interest in chronic pelvic pain conditions. CONCLUSION: Pelvic pain in younger women is a critical public health issue experienced by a significant portion of the population. Significant awareness deficits and barriers to care exist. Careful study of the barriers to receiving adequate medical care reported by these women will allow researchers to describe how best to improve care for these syndromes.

Patterns of help-seeking in women when problems arise in their sexual life: A discussion paper.
Azar M, Bradbury-Jones C, Kroll T
J Clin Nurs. 2013 Sep 13. doi: 10.1111/jocn.12374. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24028212

AIMS AND OBJECTIVES: To explore patterns of help-seeking in women who have sexual dysfunction and the implications for nursing practice. BACKGROUND: Female sexual dysfunction is a common problem that is under-reported and untreated. Barriers to help-seeking reported in existing literature relate to the perception among many women that sexual dysfunction is: part of the normal ageing process; not bothersome or does not exist; an issue that health professionals are reluctant to address; a taboo subject. However, little is known about patterns of help-seeking in women with sexual problems. This leaves a potential gap in nursing knowledge regarding appropriate, supportive strategies. DESIGN: Discursive inquiry framed theoretically by Vogel's model. METHODS: A literature review was undertaken by searching relevant databases. A combination of keywords was used to identify peer-review papers relating to women's help-seeking behavior for sexual dysfunction. Vogel's model was used as a framework to extract relevant information from the papers and structure the discussion. RESULTS: Vogel's model comprises four steps: encoding and interpreting, generating options, decision-making and evaluation of behavior. Using this stepwise approach helped elucidate the complex mechanisms associated with help-seeking in a structured manner. The key issues associated with help-seeking intention are concerned with women's personal awareness of and interaction with the environment. CONCLUSIONS: Vogel's model offers a new approach to understanding the dynamics that underpin women's decisions to seek professional help when sexual concerns arise and also provides a useful framework for nurses to consider women's specific sexual concerns. RELEVANCE TO CLINICAL PRACTICE: Implications for nursing practice are focused on public awareness, women's empowerment and the provision of effective sexual health care. Because sexual dysfunction is a global phenomenon, it is likely that the discussion in this paper will be relevant to an international, nursing readership.

Increased pressure pain sensitivity in women with chronic pelvic pain.
As-Sanie S, Harris RE, Harte SE, Tu FF, Neshewat G, Clauw DJ
Obstet Gynecol. 2013 Oct 7. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24104772

OBJECTIVE: To determine whether women with chronic pelvic pain and variable degrees of endometriosis demonstrate altered pain sensitivity relative to pain-free healthy women in a control group and whether such differences are related to the presence or severity of endometriosis or comorbid pain syndromes. METHODS: Four patient subgroups (endometriosis with chronic pelvic pain [n=42], endometriosis with dysmenorrhea [n=15], pain-free endometriosis [n=35], and chronic pelvic pain without endometriosis [n=22]) were each compared with 30 healthy women in a control group in this cross-sectional study. All patients completed validated questionnaires regarding pain symptoms and underwent screening for comorbid pain disorders. Pain sensitivity was assessed by applying discrete pressure stimuli to the thumbnail using a previously validated protocol. RESULTS: While adjusting for age and education, pain thresholds were lower in all subgroups of women with pelvic pain relative to healthy women in the control group (all P values <.01). There was no difference in pain thresholds when comparing patients with endometriosis without pelvic pain with healthy women in the control group (mean difference 0.02 kg/m, 95% confidence interval -0.43 to 0.47). The presence and severity of endometriosis and number of comorbid pain syndromes were not associated with a difference in pain thresholds. CONCLUSION: Women with chronic pelvic pain demonstrate increased pain sensitivity at a nonpelvic site compared with healthy women in a control group, which is independent of the presence or severity of endometriosis or comorbid pain syndromes. These findings support the notion that central pain amplification may play a role in the development of pelvic pain and may explain why some women with pelvic pain do not respond to therapies aimed at eliminating endometriosis lesions. LEVEL OF EVIDENCE: II.

The association of dysmenorrhea with noncyclic pelvic pain accounting for psychological factors.
Westling AM, Tu F, Griffith JW, Hellman KM
Am J Obstet Gynecol 2013 Aug 22. [Epub ahead of print.]
http://www.ncbi.nlm.nih.gov/pubmed/23973396

Objective: The factors that underlie pelvic pain are poorly understood. Specifically, the relative influence of dysmenorrhea and psychological factors in the etiology of noncyclic pelvic pain conditions, such as interstitial cystitis and irritable bowel syndrome, is unknown. To further characterize pelvic pain, we compared the frequency of menstrual, somatosensory, and psychological risk factors between women with and without severe noncyclic pelvic pain symptoms. Study design: A total of 1012 reproductive-aged women completed a 112-item questionnaire with domains including mood, fatigue, physical activity, somatic complaint, and pain. Questionnaire items included existing items for menstrual distress and newly written items derived from qualitative interviews. The relationship of dysmenorrhea and noncyclic pelvic pain complaints (dyspareunia, dyschezia, or dysuria) was modeled using quantile regression. Results: Among women who menstruate regularly, those with dysmenorrhea had disproportionally more severe noncyclic pelvic pain (54/402, 13%) than women without dysmenorrhea (5/432, 1%; odds ratio, 13; 95% confidence interval, 5–33). In a multivariate-adjusted model, dysmenorrhea (β = .17), activity capability (β = .17), somatic complaint (β = .17), and bodily pain (β = .12) were the primary predictors of noncyclic pelvic pain. Depression (β = .03) and anxiety (β = .01) were not significantly predictive. The presence of dysmenorrhea, somatic complaint, and low activity capability predicted 90% of the cases of women with noncyclic pelvic pain. Conclusion: The association between dysmenorrhea and noncyclic pelvic pain suggests that menstrual pain is an etiological factor in noncyclic pelvic pain, whereas depression and anxiety may be secondary effects. Longitudinal studies are needed to determine whether dysmenorrhea causally influences development of noncyclic pelvic pain or shares common underlying neural mechanisms.

Incidence of genitourinary conditions in women with a diagnosis of vulvar/vaginal atrophy.
Constantine GD, Bruyniks N, Princic N, Huse D, Palmer L, Lenhart G, Blumentals WA, Nappi RE
Curr Med Res Opin. 2013 Oct 1. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24083677

Abstract Objectives: Vulvar/vaginal atrophy (VVA) is one genitourinary condition associated with a decline in estrogen. This may be bothersome for women following menopause. Although the clinical features of VVA and other conditions after menopause have been documented, few studies have quantified the magnitude of association between VVA and other genitourinary conditions. Methods: A VVA cohort was identified from two United States administrative claims databases. A matched cohort of an equal number of controls was randomly selected from a pool of women 40-79 years of age without VVA. Baseline characteristics and medical history were tabulated for the VVA cohort and matched controls. Six genitourinary conditions ('urinary tract infections', 'other/unspecified genitourinary symptoms', 'other inflammatory diseases of female pelvic organs', 'menopausal disorders', 'female genital pain and other symptoms', and 'other/unspecified female genital disorders') were hypothesized a priori to be associated with VVA. Adjusted incidence rate ratios measured the strength of association of VVA with each condition. Results: 9,080 women aged 40-79 years with newly diagnosed VVA during 2000-2010 were identified. The mean age of VVA patients and matched controls was 60.2 years. At baseline, a significantly ($p<0.001$) higher proportion of women in the VVA cohort had a diagnosis of angina, osteoporosis, migraines, insomnia, or anxiety, or received estrogen supplementation or selective estrogen receptor modulators. VVA patients had a significantly ($p<0.001$) higher incidence of each of the genitourinary conditions compared to controls. The condition most strongly associated with VVA with a relative risk of 6.2 was 'other inflammatory diseases of female pelvic organs'. Conclusions: Women with VVA have a greater risk of genitourinary conditions compared to those without. That the overall prevalence of VVA and other genitourinary conditions may be underreported as claims data only captures information for patients under medical care and many women do not seek consultation for VVA symptoms.

Histopathologic characteristics of menopausal vestibulodynia.
Leclair CM, Goetsch MF, Li H, Morgan TK
Obstet Gynecol. 2013 Oct;122(4):787-793.
http://www.ncbi.nlm.nih.gov/pubmed/24084535

OBJECTIVE: To assess whether premenopausal and postmenopausal vestibulodynia have different histologic features. METHODS: We conducted a retrospective analysis of vestibulectomy specimens from 21 women with postmenopausal vestibulodynia and compared them with 88 premenopausal patients (42 primary, 46 secondary). Women with primary vestibulodynia experienced pain at first introital touch and women with secondary vestibulodynia experienced pain after an interval of painless intercourse. Clinical records established the type of vestibulodynia, duration of symptoms, and hormone status. Tissues were stained for inflammation, nerves, mast cells, estrogen receptor α, and progesterone receptor. Histologic findings in the postmenopausal patients were compared with primary and secondary premenopausal patients using proportional odds logistic regression and analysis of variance. RESULTS: Seventy-one percent (15/21) of postmenopausal women reported vestibular dyspareunia related to a drop in estrogen either with menopause (13/21) or previously, postpartum (2/21). Eighty-six percent (18/21) of postmenopausal patients were using local or systemic estrogen but pain persisted. Compared with premenopausal primary and secondary vestibular biopsies, postmenopausal tissues had more lymphocytes (unadjusted odds ratio [OR] 9.0, 95% confidence interval [CI] 2.8-33.3; adjusted OR for parity and duration of symptoms 9.1, 95% CI 2.6-31.9; unadjusted OR 6.2, 95% CI 1.9-20.0; adjusted OR 6.6, 95% CI 2.0-21.9, respectively) and mast cells (mean 36 compared with 28 and 36 compared with 26, respectively). There was significantly less neural hyperplasia and progesterone receptor expression in postmenopausal biopsies compared with primary cases but less progesterone receptor and similar neural hyperplasia compared with premenopausal secondary cases. Estrogen receptor α did not vary among groups. CONCLUSION: Premenopausal and postmenopausal vestibulodynia share histologic features of neurogenic inflammation but differ strikingly in degree. When estrogen supplement does not alleviate symptoms of postmenopausal dyspareunia, vestibulodynia should be considered. LEVEL OF EVIDENCE: II.

A comparison of demographic and psychosexual characteristics of women with primary versus secondary provoked vestibulodynia.
Brotto LA, Sadownik LA, Thomson S, Dayan M, Smith KB, Seal BN, Moses M, Zhang A
Clin J Pain. 2013 Jul 24. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23887337

OBJECTIVES: Provoked vestibulodynia (PVD) is a distressing genital pain condition affecting approximately 12% of premenopausal women. It has been speculated that primary (ie, lifelong) and secondary (ie, acquired) PVD may represent 2 distinct conditions with different etiologies. There is also evidence that primary and secondary PVD subtypes may respond differently to conventional treatments. The goal of this study was to compare the demographic, clinical, and psychosexual characteristics of a large sample of premenopausal women with primary and secondary PVD. METHODS: A total of 132 premenopausal women (n=42 primary; n=90 secondary) with PVD who sought treatment in a Multidisciplinary Vulvodynia Program completed demographic questions and a battery of validated self-report measures before treatment. RESULTS: Women with primary PVD had a longer duration of PVD as well as more time before diagnosis. Women with secondary PVD reported significantly more clitoral hood pain, higher overall vestibular pain levels, more overall sexual dysfunction and sex-related distress, and proportionately more intercourse occasions that were painful. Women with primary pain stated they had significantly more dysmenorrhea and were more likely to report that their partners were unaware of their PVD symptoms. There were no significant subtype differences on any psychological measure but a trend towards higher magnification of symptoms in women with secondary PVD. DISCUSSION: Overall the findings suggest some important differences in the characteristics of women with primary versus secondary PVD which may have management-related implications.

Women with provoked vestibulodynia experience clinically significant reductions in pain regardless of treatment: Results from a 2-year follow-up study.

Davis SN, Bergeron S, Binik YM, Lambert B

J Sex Med. 2013 Sep 12. doi: 10.1111/jsm.12309. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24034424

INTRODUCTION: Provoked vestibulodynia (PVD) is a prevalent genital pain syndrome that has been assumed to be chronic, with little spontaneous remission. Despite this assumption, there is a dearth of empirical evidence regarding the progression of PVD in a natural setting. Although many treatments are available, there is no single treatment that has demonstrated efficacy above others. AIMS: The aims of this secondary analysis of a prospective study were to (i) assess changes over a 2-year period in pain, depressive symptoms, and sexual outcomes in women with PVD; and (ii) examine changes based on treatment(s) type. METHODS: Participants completed questionnaire packages at Time 1 and a follow-up package 2 years later. MAIN OUTCOME MEASURES: Visual analog scale of genital pain, Global Measure of Sexual Satisfaction, Female Sexual Function Index, Beck Depression Inventory, Dyadic Adjustment Scale, and sexual intercourse attempts over the past month. RESULTS: Two hundred thirty-nine women with PVD completed both time one and two questionnaires. For the sample as a whole, there was significant improvement over 2 years on pain ratings, sexual satisfaction, sexual function, and depressive symptoms. The most commonly received treatments were physical therapy, sex/psychotherapy, and medical treatment, although 41.0% did not undergo any treatment. Women receiving no treatment also improved significantly on pain ratings. No single treatment type predicted better outcome for any variable except depressive symptoms, in which women who underwent surgery were more likely to improve. DISCUSSION: These results suggest that PVD may significantly reduce in severity over time. Participants demonstrated clinically significant pain improvement, even when they did not receive treatment. Furthermore, the only single treatment type predicting better outcomes was surgery, and only for depressive symptoms, accounting for only 2.3% of the variance. These data do not demonstrate the superiority of any one treatment and underscore the need to have control groups in PVD treatment trials, otherwise improvements may simply be the result of natural progression.

Anticonvulsant pharmacotherapy for generalized and localized vulvodynia: a critical review of the literature.

Spoelstra SK, Borg C, Weijmar Schultz WC

J Psychosom Obstet Gynaecol. 2013 Sep;34(3):133-8. doi: 10.3109/0167482X.2013.823942.
http://www.ncbi.nlm.nih.gov/pubmed/23952171

Anticonvulsant therapy has occasionally been recommended to treat vulvodynia. However, convincing evidence to support this therapeutic option is lacking. The goal of this study was to critically review studies published on the effectiveness of anticonvulsants for the treatment of vulvodynia. Evaluation of the methodological quality of relevant publications was the main outcome measure. MEDLINE, PubMED and Cochrane were used to identify studies published in English between January 1999 and February 2013. Searches were performed between December 2012 and February 2013. Articles were appraised with the Oxford Centre for Evidence-Based Medicine - Levels of Evidence. Eight relevant studies were identified: two case reports, three retrospective studies, two non-randomized prospective studies and one open-label pilot trial study. Gabapentin formed the main focus (87.5%) to reduce vulvar pain; success rates ranged from 50 to 82%. Lamotrigine was used in one study (12.5%) to relieve symptoms; satisfaction was reported in 82%. These results seem promising, but the majority of studies have several methodological weaknesses regarding sample size and design. Insufficient evidence was available to recommend anticonvulsants for the treatment of vulvodynia. Further studies are necessary with double-blind, randomized-controlled designs to investigate the effectiveness of anticonvulsant therapy for vulvodynia.

Vulvodynia and fungal association: a preliminary report.
Ventolini G, Gygax SE, Adelson ME, Cool DR
Med Hypotheses. 2013 Aug;81(2):228-30. doi: 10.1016/j.mehy.2013.04.043.
http://www.ncbi.nlm.nih.gov/pubmed/23707510

Vulvodynia (vulvar pain syndrome) is a chronic multifactorial disease affecting almost 13 million women in the USA and can lead to morbidity and a reduced quality of life. We hypothesize that an initial microbiological insult in the vagina causes modifications in the biological vaginal milieu and/or an alteration on the lactobacilli flora. The vaginal milieu responds to the insult by developing an inflammatory reaction with abnormal cytokine production. These hypotheses were tested quantifying vaginal lactobacillus and cytokines, in patients with vulvodynia compared to matched healthy controls. Our preliminary data suggest a vaginal flora alteration and an immunological response involving Candida in patients with vulvodynia. Ongoing studies will assist us to clarify these findings.

Vulvodynia: An unrecognized diabetic neuropathic syndrome.
Kalra B, Kalra S, Bajaj S
Indian J Endocrinol Metab. 2013 Sep;17(5):787-789.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3784859/

Vulvar pain syndromes, including vulvodynia, are a common source of morbidity in women and cause much physical and psychological suffering. This brief communication postulates the hypothesis that unexplained vulvar pain may be hitherto undescribed manifestation of painful sensory diabetic neuropathy. It describes the clinical characteristics of vulvodynia and highlights the similarities between this condition and diabetic neuropathy. The hypothesis calls for women presenting with vulvar pain to be screened for diabetes, as well as women with diabetes to be questioned about vulvar symptomatology. The paper hopes to stimulate extensive research in this important, but so far neglected, field of women's endocrine health.

Outcome measures for vulval skin conditions: a systematic review of randomized controlled trials.
Simpson RC, Thomas KS, Murphy R
Br J Dermatol. 2013 Sep;169(3):494-501. doi: 10.1111/bjd.12391.
http://www.ncbi.nlm.nih.gov/pubmed/23600623

Symptoms and signs of vulval skin disorders are common. These conditions can have a considerable impact on quality of life, restricting physical activities and causing difficulty in everyday activities and may also affect social, psychosexual and psychological well-being. There are no standardized measures routinely used to assess the impact of vulval disease on daily life. To report outcome measures used in clinically based randomized controlled trials (RCTs) investigating therapeutic interventions in vulval disease. The Medline, EMBASE and CENTRAL databases were searched to identify RCTs of vulval skin conditions written in English. Studies with laboratory tests or survival rates as the primary outcome, or those investigating menopausal symptoms or infections were excluded. Twenty-eight published RCTs were included. The vulval conditions represented were vulvodynia (n = 14), lichen sclerosus (n = 9), vulval intraepithelial neoplasia (n = 2), vulval pruritus (n = 2) and lichen planus (n = 1). The 28 RCTs measured 25 different outcomes, using 49 different scales. The method of outcome assessment was lacking on nine occasions. Only 21% (six of 28) of included trials had a clearly stated primary outcome. Patient-reported outcomes were more commonly reported than clinician-related outcome measures. The most commonly reported patient-rated outcome measure was a reduction in pain (measured 15 times) and an overall improvement in symptoms using a patient global assessment (measured 11 times). The most commonly reported clinician-rated outcome was an overall assessment of the appearance of affected sites (measured 13 times). There were no agreed standard scales used for the global assessments. Only nine of the recorded outcome measure tools were designed to assess vulval disease or sexual functioning, the remainder were general measures. There is heterogeneity in the outcome measures used when reporting therapeutic interventions in vulval disease. This field of dermatology would benefit from development of a vulval-specific outcome measure and the establishment of a core outcome measure set.

Interpretation of the sexual functioning questionnaire in the presence of vulvar pain.
Legocki LJ, Aikens JE, Sen A, Haefner HK, Reed BD
J Low Genit Tract Dis. 2013 Jul;17(3):273-9. doi: 10.1097/LGT.0b013e31826ca384.
http://www.ncbi.nlm.nih.gov/pubmed/23595036

OBJECTIVE: This study aimed to assess whether the domains identified by items on the Sexual Functioning Questionnaire (SFQ) apply to women with vulvodynia. MATERIALS AND METHODS: Forty-one women with vulvodynia and 43 asymptomatic controls, between the ages 18 and 70 years, were assessed with a physician evaluation and a written survey that included the SFQ. RESULTS: Women with vulvodynia had a higher likelihood of female sexual dysfunction than did controls as indicated by 5 of the seven individual SFQ domains (desire, arousal-lubrication, pain, enjoyment, and partner domains, $p < .05$). Scored on individual items relating to pain or penetrative sex differed more by vulvodynia presence than did items related to arousal and emotions. Compared with published SFQ psychometrics, factor analysis among women with vulvodynia demonstrated similar factor loadings in 6 of the 7 domains of the SFQ (desire, arousal-sensation, arousal-lubrication, orgasm, partner, and pain), but the enjoyment domain intermingled substantially with these other domains. CONCLUSIONS: The SFQ factor structure is generally valid among women with vulvodynia. However, vulvodynia may impact responses to individual items on questions about pain and/or penetration, which may potentially result in erroneous interpretations.

2013 vulvodynia update.
[Article in French]
de Belilovsky C
Gynecol Obstet Fertil. 2013 Sep;41(9):505-10. doi: 10.1016/j.gyobfe.2013.06.008.
http://www.ncbi.nlm.nih.gov/pubmed/23972919

Provoked vestibulodynia represents the most frequent cause of dyspareunia before menopause. Vulvodynia's pain and burning sensations are related to neuropathic pain and associated to various degrees of vulvar mucosal hypersensitivity (mostly in the vestibular area), pelvic floor muscles dysfunction, a disorder of general perception of pain and/or various complex regional pain syndromes such as fibromyalgia, glossodynia, painful bladder syndrome (interstitial cystitis)… Vaginal infections such as candidiasis and vaginosis are important trigger and risk factors. Women suffering from vulvodynia are often described as vulnerable, pessimistic, developing feelings of guilt towards their partner. They tend to be hyper vigilant to their pain and develop catastrophizing reactions (rumination, magnification and helplessness) and avoidance/escape behaviors (fear-avoidance model). Diagnosis is based on medical history, clinical examination (Q-tip test) and exclusion of vaginitis. Treatment consists of a multidisciplinary approach involving topical therapies (emollients, anesthetics, hormonotherapy if necessary), pelvic floor physiotherapy with electromyographic biofeedback, drug treatment of pain with antidepressants (amitriptyline…) or anticonvulsants (pregabalin…) and a psychosexual support.

Terminology and diagnosis of vulval pain.
Maclean AB, Siddiqui G.
J Obstet Gynaecol. 2013 Oct;33(7):651-4. doi: 10.3109/01443615.2013.825585.
http://www.ncbi.nlm.nih.gov/pubmed/24127946

Accurate terminology to allow meaningful understanding of aetiology, diagnosis and management of vulval pain continues to evolve. The most recent classification has been endorsed by the International Society for the Study of Vulvovaginal Disease, and is discussed. In theory, we should replace 'vulvodynia' by 'aidoiodynia', as per this issue's associated Editorial.

Persistent genital arousal and restless genitalia: sexual dysfunction or subtype of vulvodynia?
Markos A, Dinsmore W
Int J STD AIDS. 2013 Aug 1. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23970620

We conducted a literature review of patients' conditions described under persistent genital arousal disorder and restless genital syndrome, vulvodynia and male genital skin pain of unknown aetiology (penoscrotodynia). Our aim is to improve the understanding of the condition, unify nomenclature and promote evidence-based practice. The most prominent symptom in persistent genital arousal disorder and restless genital syndrome is the spontaneous, unwelcomed, intrusive and distressing vulval sensation. There are similarities between the clinical presentation of vulvodynia, penoscrotodynia, persistent genital arousal disorder and restless genital syndrome patients. The aetiology of persistent genital arousal disorder and restless genital syndrome, similar to vulvodynia, could be better explained in terms of neuro-vascular dysfunction, genital peripheral neuropathy and/or dysfunctional micro-vascular arterio-venous shunting. Erythromelalgia lends itself to explain some cases of restless genital syndrome, who have concurrent restless leg syndrome; and therefore draw parallels with red scrotum syndrome. The published literature support the concept of classifying restless genital syndrome as a sub-type of vulvodynia than sexual dysfunction.

Radiofrequency therapy for severe idiopathic vulvodynia.
Kestřánek J, Spaček J, Ryška P, Adamkov J, Matula V, Buchta V
J Low Genit Tract Dis. 2013 Jul 30. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23903198

OBJECTIVE: The study aimed to provide a description of a new and a hopeful possibility in the treatment of severe vulvodynia, which does not respond to treatments used so far. MATERIALS AND METHODS: The use of radiofrequency therapy in vulvodynia treatment is described for the first time. This method was suggested by a neurosurgeon after applying all available possibilities. RESULT: In this article, we are reporting on the successful use of the pulsed radiofrequency treatment in a patient with intractable chronic vulvodynia. CONCLUSIONS: To our knowledge, this is the first report of a successful use of pulsed radiofrequency in the treatment of chronic vulvodynia. If efficacy of pulsed radiofrequency is confirmed by more studies, it would be a welcome addition to the treatment modalities used to treat this sometimes truly intractable condition.

Central sensitization in urogynecological chronic pelvic pain: A systematic literature review.
Kaya S, Hermans L, Willems T, Roussel N, Meeus M
Pain Physician. 2013 Jul-Aug;16(4):291-308.
http://www.ncbi.nlm.nih.gov/pubmed/23877446

BACKGROUND: Chronic pelvic pain (CPP) is a complex pain syndrome. Since its pathogenesis is still poorly understood and structural alterations in pain related brain regions may be present, there is a greater acceptance that sensitization of the central nervous system (CNS) plays an important role in the development and maintenance of chronicity. OBJECTIVE: The purpose of this study is to systematically review the scientific evidence regarding central sensitization (CS) in female patients with urogynecological CPP. STUDY DESIGN: Systematic review of the literature. METHODS: A systematic literature search was conducted in PubMed and Web of Science using different keyword combinations related to urogynecological CPP and central sensitization. Full text clinical reports addressing CS in adult women with urogynecological CPP were included and assessed for methodological quality by 2 independent reviewers. RESULTS: After screening for the eligibility, a total of 29 full-text articles with low to good methodological quality were retained. All studies were observational, 27 of which were case-control and 2 of which were cohorts. Sensitivity of the CNS was investigated by using a variety of methods. Although different central mechanisms seem to be involved in pain processing, the present evidence suggests hyperexcitability of the CNS in patients with urogynecological CPP. Altered brain morphology and function, generalized hyperalgesia to different type of stimuli, overactive bottom-up nociceptive mechanisms, and autonomic dysregulation were established in patients with urogynecological CPP. Nevertheless, diffuse noxious inhibitory control seemed normal, and therefore the contribution of an impaired

endogenous pain inhibition mechanism to CPP requires further study. The same goes for the contribution of psychological factors. LIMITATIONS: The level of evidence of retained studies is low due to the observational study designs and a wide range of diagnoses and assessment methods. CONCLUSION: Although the majority of the literature provides evidence for the presence of CS in urogynecological CPP with changes in brain morphology/function and sensory function, it is unclear whether these changes in central pain processing are secondary or primary to CPP, especially since evidence regarding the function of endogenous pain inhibition and the role of psychosocial pain facilitation is scarce. Further studies with good methodological quality are needed in order to clarify exact mechanisms.

The 2013 EAU guidelines on chronic pelvic pain: Is management of chronic pelvic pain a habit, a philosophy, or a science? 10 years of development.

Engeler DS, Baranowski AP, Dinis-Oliveira P, Elneil S, Hughes J, Messelink EJ, van Ophoven A, Williams AC
Eur Urol. 2013 Sep;64(3):431-9. doi: 10.1016/j.eururo.2013.04.035.
http://www.ncbi.nlm.nih.gov/pubmed/23684447

CONTEXT: Progress in the science of pain has led pain specialists to move away from an organ-centered understanding of pain located in the pelvis to an understanding based on the mechanism of pain and integrating, as far as possible, psychological, social, and sexual dimensions of the problem. This change is reflected in all areas, from taxonomy through treatment. However, deciding what is adequate investigation to rule out treatable disease before moving to this way of engaging with the patient experiencing pain is a complex process, informed by pain expertise as much as by organ-based medical knowledge. OBJECTIVE: To summarize the evolving changes in the management of patients with chronic pelvic pain by referring to the 2012 version of the European Association of Urology (EAU) guidelines on chronic pelvic pain. EVIDENCE ACQUISITION: The working panel highlights some of the most important aspects of the management of patients with chronic pelvic pain emerging in recent years in the context of the EAU guidelines on chronic pelvic pain. The guidelines were completely updated in 2012 based on a systematic review of the literature from online databases from 1995 to 2011. According to this review, levels of evidence and grades of recommendation were added to the text. A full version of the guidelines is available at the EAU office or Web site (www.uroweb.org). EVIDENCE SYNTHESIS: The previously mentioned issues are explored in this paper, which refers throughout to dilemmas for the physician and treatment team as well as to the need to inform and engage the patient in a collaborative empirical approach to pain relief and rehabilitation. These issues are exemplified in two case histories. CONCLUSIONS: Chronic pelvic pain persisting after appropriate treatment requires a different approach focusing on pain. This approach integrates the medical, psychosocial, and sexual elements of care to engage the patient in a collaborative journey towards self-management.

Magnetic resonance imaging of the pelvic floor: From clinical to biomechanical imaging.

Brandão S, Roza TD, Parente M, Ramos I, Mascarenhas T, Natal Jorge RM
Proc Inst Mech Eng H. 2013 Sep 12. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24030164

This article reviews the current role of magnetic resonance imaging in the study of the pelvic floor anatomy and pelvic floor dysfunction. The application of static and dynamic magnetic resonance imaging in the clinical context and for biomechanical simulation modeling is assessed, and the main findings are summarized. Additionally, magnetic resonance-based diffusion tensor imaging is presented as a potential tool to evaluate musclefiber morphology. In this article, focus is set on pelvic floor muscle damage related to urinary incontinence and pelvic organ prolapse, sometimes as a consequence of vaginal delivery. Modeling applications that evaluate anatomical and physiological properties of pelvic floor are presented to further illustrate their particular characteristics. Finally, finite element method is described as a method for modeling and analyzing pelvic floor structures' biomechanical performance, based on material and behavioral properties of the tissues, and considering pressure loads that mimic real-life conditions such as active contraction or Valsalva maneuver.

Pelvic floor dysfunction: Does menopause duration matter?
Trutnovsky G, Guzman-Rojas R, Martin A, Dietz HP
Maturitas. 2013 Oct;76(2):134-8. doi: 10.1016/j.maturitas.2013.06.012.
http://www.ncbi.nlm.nih.gov/pubmed/23860336

OBJECTIVE: To explore the effect of menopause and hormone replacement therapy on pelvic organ prolapse and pelvic floor muscle function. METHODS: The records of patients who attended a tertiary urogynaecological center were reviewed retrospectively. A standardised interview included menopausal age, i.e. years since last period or onset of menopausal symptoms, current or previous hormone use. The clinical examination included prolapse assessment (POP-Q) and palpation of the levator ani muscle. 4D transperineal ultrasound, supine and after voiding, was performed in all patients. Volume data sets were analysed for pelvic organ descent and measures of contractility and distensibility of the pelvic floor at a later date, blinded to all clinical data. RESULTS: Of 311 women seen during the inclusion period, 65% were postmenopausal. Current systemic or local hormone use was reported by 7% and 6%, respectively. 163 women (52%) reported prolapse symptoms with a mean bother of 5.7/10. Significant pelvic organ prolapse was found on clinical examination (POP-Q stage≥2) in 77%, and diagnosed on ultrasound in 61%. On multivariate analysis, controlling for calendaric age, parity and levator avulsion, there was no evidence for menopausal age as an independent predictor of any symptom and sign of pelvic organ prolapse and pelvic floor muscle function. Local oestrogen use and past or present hormone replacement therapy had no detectable effect on any pelvic floor parameter. CONCLUSIONS: Hormone deficiency following menopause is unlikely to play a major role in pelvic organ support and levator ani function. Hence, both do not appear to be substantially influenced by local or systemic hormone replacement therapy.

Do romantic partners' responses to entry dyspareunia affect women's experience of pain? The roles of catastrophizing and self-efficacy.
Lemieux AJ, Bergeron S, Steben M, Lambert B
J Sex Med. 2013 Sep;10(9):2274-84. doi: 10.1111/jsm.12252.
http://www.ncbi.nlm.nih.gov/pubmed/23809759

INTRODUCTION: Entry dyspareunia is a sexual health concern which affects about 21% of women in the general population. Characterized by pain provoked during vaginal penetration, introital dyspareunia has been shown by controlled studies to have a negative impact on the psychological well-being, sexual function, sexual satisfaction, and quality of life of afflicted women. Many cognitive and affective variables may influence the experience of pain and associated psychosexual problems. However, the role of the partner's cognitive responses has been studied very little. AIM: The aim of the present study was to examine the associations between partners' catastrophizing and their perceptions of women's self-efficacy at managing pain on one side and women's pain intensity, sexual function, and sexual satisfaction on the other. METHODS: One hundred seventy-nine heterosexual couples (mean age for women = 31, SD = 10.0; mean age for men = 33, SD = 10.6) in which the woman suffered from entry dyspareunia participated in the study. Both partners completed quantitative measures. Women completed the Pain Catastrophizing Scale and the Painful Intercourse Self-Efficacy Scale. Men completed the significant-other versions of these measures. MAIN OUTCOME MEASURES: Dependent measures were women's responses to (i) the Pain Numeric Visual Analog Scale; (ii) the Female Sexual Function Index; and (iii) the Global Measure of Sexual Satisfaction scale. RESULTS: Controlled for women's pain catastrophizing and self-efficacy, results indicate that higher levels of partner-perceived self-efficacy and lower levels of partner catastrophizing are associated with decreased pain intensity in women with entry dyspareunia, although only partner catastrophizing contributed unique variance. Partner-perceived self-efficacy and catastrophizing were not significantly associated with sexual function or satisfaction in women. CONCLUSIONS: The findings suggest that partners' cognitive responses may influence the experience of entry dyspareunia for women, pointing toward the importance of considering the partner when treating this sexual health problem.

CT-guided percutaneous pulse-dose radiofrequency for pudendal neuralgia.
Masala S, Calabria E, Cuzzolino A, Raguso M, Morini M, Simonetti G
Cardiovasc Intervent Radiol. 2013 Aug 21. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23963376

PURPOSE: The purpose of our study was to evaluate the efficacy of computed tomography (CT)-guided percutaneous pulse-dose radiofrequency (PDRF) for the treatment of chronic pain in patients with pudendal neuralgia (PN) unresponsive to conservative approaches. METHODS: From March 2010 to January 2012, 30 patients with a diagnosis of PN were prospectively enrolled in the study, 18 women and 12 men (mean age 47 years). A 20-gauge cannula with a 10-cm length was placed under CT guide in the pudendal (Alcock's) canal. After the spindle was removed, a radiofrequency needle with a 5-mm active tip was introduced. The appropriate needle placement near the pudendal nerve, without an involvement of the vessels, was confirmed with an injection of 1-2 ml of contrast agent. PDRF was performed with 1,200 pulses at high voltage (45 V) with 20 ms duration followed by 480 ms silent phases. RESULTS: Twenty-six patients completed the study. Procedural success was achieved in all patients. Mean VAS scores before PDRF was 9 ± 0.7. Patients had a great improvement in pain intensity after 1 week by PDRF (mean VAS scores 3.8 ± 1.7, $p < 0.05$), with a stabilization of the symptomatology in the following months (mean VAS scores 1.5 ± 1.1 at 6 months by PDRF, $p < 0.05$) and excellent results after 1 year by the procedure (mean VAS scores 1.9 ± 0.7, $p < 0.05$). CONCLUSIONS: In our preliminary experience, CT-guided percutaneous PDRF should be recommended for treatment of PN because we evaluated the tolerability of this procedure with satisfactory and encouraging results.

Pudendal nerve palsy in trauma and elective orthopaedic surgery.
Polyzois I, Tsitskaris K, Oussedik S
Injury. 2013 Sep 8. pii: S0020-1383(13)00388-4. doi: 10.1016/j.injury.2013.09.001. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24054001

The incidence of pudendal nerve palsy following routine trauma and elective orthopaedic surgery procedures ranges from 1.9% to 27.6%. Excessive and/or prolonged traction against the perineal post of a traction table, leading to direct compression and localised ischaemia to the nerve are suggested mechanisms of injury. Misuse of traction and the inappropriate placement of the perineal post, leading to crushing and stretching of the pudendal nerve, are two main contributing factors leading to its postoperative palsy. The sequelae may be sensory, motor or mixed. In most cases, these injuries are transient and tend to resolve within several weeks or months. However, complete neurological recovery may be unpredictable and the effects of ongoing dysfunction potentially disastrous for the individual. In terms of preventative measures, magnitude and duration of traction time should be minimized; traction should be limited to the critical operative steps only. Additionally, the perineal post should be placed between the genitalia and the contralateral leg. A well-padded, large-diameter perineal post should be used (>10cm). Adequate muscle relaxation during anaesthesia is particularly important in young men who have strong muscles and thus require larger traction forces when compared to elderly patients. Orthopaedic surgeons should be aware of the pathophysiology behind the development of this palsy and the measures that can be employed to reduce its occurrence. In procedures where a traction table is employed, consenting for pudendal nerve palsy should be considered by the surgical team.

Pudendal nerve neuralgia after hip arthroscopy: Retrospective study and literature review.
Pailhé R, Chiron P, Reina N, Cavaignac E, Lafontan V, Laffosse JM
Orthop Traumatol Surg Res. 2013 Sep 27. pii: S1877-0568(13)00175-8. doi: 10.1016/j.otsr.2013.07.015. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24080353

INTRODUCTION: Pudendal nerve neurapraxia is a classic complication after traction on the fracture table. Diagnosis, however, is difficult and often overlooked, especially after arthroscopy in traction on fracture table; incidence is therefore not known exactly. HYPOTHESIS: The study hypothesis was that incidence of pudendal nerve neuropathy exceeds 1% after hip arthroscopy. MATERIALS AND METHODS: Results for 150 patients (79 female, 71 male) undergoing hip arthroscopy between 2000 and 2010 were analyzed retrospectively. The principal assessment criterion was onset

of pudendal neuralgia. Secondary criteria were risk factors (history, surgery time, type of anesthesia), associated complications, onset to diagnosis interval and pattern of evolution. RESULTS: At a mean 93 months' follow-up, there were 3 cases (2 women, 1 man) (2%) of pure sensory pudendal neuralgia; 2 concerned labral lesion resection and 1 osteochondromatosis. Surgery time ranged from 60 to 120min, under general anesthesia with curarization. Time to diagnosis was 3 weeks. No complementary examinations were performed. Spontaneous resolution occurred at 3 weeks to 6 months. No significant risk factors emerged. CONCLUSION: The present study found 2% incidence of pudendal neuralgia, with no risk factors emerging from analysis. Prevention involves limiting traction force and duration by using a large pelvic support (diameter>8-10cm). Patient information and postoperative screening should be systematic. LEVEL OF EVIDENCE: Level IV. Retrospective study.

A critique of current practice of transvaginal pudendal nerve blocks: a prospective audit of understanding and clinical practice.

Ford JM, Owen DJ, Coughlin LB, Byrd LM

J Obstet Gynaecol. 2013 Jul;33(5):463-5. doi: 10.3109/01443615.2013.771155.

http://www.ncbi.nlm.nih.gov/pubmed/23815197

Pudendal nerve blocks are a pre-requisite to forceps delivery without regional anaesthesia. Their efficacy is dependent on introducing local anaesthetic in close proximity to the pudendal nerve and allowing sufficient time for its onset of action. An audit of 57 obstetricians evaluated their clinical technique against standards using both a questionnaire and adapted model pelvis. The majority of participants were unable to describe correctly the point of infiltration and were unaware of the lag time required to effect adequate analgesia. We identify a deficiency in training and describe a method by which training can be facilitated and assessed.

Contemporary treatment of sexual dysfunction: Reexamining the biopsychosocial model.

Berry MD, Berry PD

J Sex Med. DOI: 10.1111/jsm.12273. Article first published online: 12 AUG 2013

http://www.ncbi.nlm.nih.gov/pubmed/23937720

Introduction: The introduction of phosphodiesterase type 5 inhibitors has revolutionized the armamentarium of clinicians in the field of sexual medicine. However, pharmacotherapy as a stand-alone treatment option has been criticized, particularly by psychosocial therapists, as incomplete. Specifically, it is widely argued that drug treatment alone often does not meet the standards of biopsychosocial (BPS) therapy. Aim: A literature review was performed to explore the role of the biopsychosocial paradigm in the treatment of sexual dysfunction and outline some of the key challenges and possible shortcomings in the current application of biopsychosocial treatment. Main Outcome Measure: Published treatment outcomes of integrative biopsychosocial clinical practice, including medical outcomes, psychological and relational factors, treatment of comorbid conditions, cost of treatment, and treatment efficacy, were investigated. Methods: Using Medline, PubMed, and EMBASE databases, a literature search for articles published from January 1, 1980, to March 1, 2013, was performed, examining current approaches to the biopsychosocial model of sexual dysfunction and sexual medicine. Data were reviewed and combined, allowing characterization of current treatment approaches and recommendations for clinical practice and future research. Results: The biopsychosocial model of treatment appears to have an intuitively obvious meaning (i.e., treatment of all three facets of the patient's biological–psychological–social condition). However, research suggests that clear treatment algorithms are still in development. By virtue of the ongoing development of biopsychosocial methods in sexual medicine, new models and research initiatives may be warranted. The evidence identified allows for characterization of some of the current clinical, professional, financial, and systemic challenges to biopsychosocial treatment, with the aim of helping identify possible directions for future research. Conclusion: Implementation of biopsychosocial treatment, though mandated by process-of-care guidelines, may be limited in the field of sexual health owing to resource limitations, limitations in physician training curricula, and structural obstacles preventing interdisciplinary collaboration. Nonetheless, a number of current treatment developments are biopsychosocially integrative, and a number of established models are biopsychosocially informed. These models and concrete strategies may provide a way forward for developing further initiatives to advance BPS treatment.

Managing female sexual dysfunction.
Buster JE
Fertil Steril. 2013 Oct;100(4):905-15. doi: 10.1016/j.fertnstert.2013.08.026.
http://www.ncbi.nlm.nih.gov/pubmed/24074537

Female sexual dysfunctions (FSDs) range from short-term aggravations to major emotional disturbances adversely affecting family and workplace. This review highlights diagnosis and management of the four most widely diagnosed FSDs. It initially focuses on hypoactive sexual desire disorder (HSDD) as a driving force at the heart of all other FSDs; nothing happens without sexual desire. Successful resolution of HSDD frequently facilitates resolution of other disorders. Central to understanding HSDD is the impact of aging female sexual endocrinology and its effect on both prevalence and expression patterns of FSD. Advances in this field have enabled introduction of some the most effective treatments yet described for HSDD. Sexual arousal disorder, though commonly affected by the same factors as HSDD, is heavily associated with psychotropic drugs and mood elevators. Orgasmic disorder is frequently the downstream result of other sexual dysfunctions, particularly HSDD, or the result of a major psychosexual trauma. Successful management of the underlying disorder often resolves orgasmic disorder. Sexual pain disorder is frequently the result of a gynecologic disorder, such as endometriosis, that can be substantially managed through successful treatment of that disorder. This article ends with the article's most important note: how to initiate the conversation.

Arriving at the diagnosis of female sexual dysfunction.
Latif EZ, Diamond MP
Fertil Steril. 2013 Oct;100(4):898-904. doi: 10.1016/j.fertnstert.2013.08.006.
http://www.ncbi.nlm.nih.gov/pubmed/24012196

Female sexual dysfunctions include a group of sexual complaints and disorders affecting women of all ages, and stemming from a heterogeneous array of etiologies and contributing factors. The classification system for sexual dysfunctions in the woman has evolved from a linear categorization of sexual desire, arousal, orgasm, and pain disorders to one that is more complex and overlapping. Personal distress is a key factor in defining a sexual problem as a dysfunction. The recently released Diagnostic and Statistical Manual of Mental Disorders, edition 5, collapses former definitions of female sexual disorders and moves away from the older linear model of diagnostic categories. Physicians should be open to discussing sexual problems with women, and may make use of validated questionnaires in the office setting. Evaluation tools available for assessing sexual function in the woman are in use in the research setting, as are physiological measures of assessment.

Sex therapy for female sexual dysfunction.
Pereira VM, Arias-Carrión O, Machado S, Nardi AE, Silva AC
Int Arch Med. 2013 Sep 26;6(1):37. [Epub ahead of print]
http://www.intarchmed.com/content/6/1/37

INTRODUCTION: About 45% of women suffer from some form of sexual dysfunction. Despite its high prevalence, there are few studies that have systematically evaluated sex therapy in comparison with other interventions. OBJECTIVE: Review randomized clinical trials that present psychotherapeutic interventions for female sexual dysfunctions. METHOD: Through a search in three databases (Medline, Web of Science and PsycInfo), 1419 references were found. After an analysis of the abstracts, twenty-seven articles met the inclusion criteria and composed this review. RESULTS: Sex therapy, as proposed by Masters and Johnson and Heiman and LoPiccolo, is still the most commonly used form of therapy for sexual dysfunctions; although it has shown results, the results do not consistently support that this is the best alternative in the treatment of sexual dysfunctions. CONCLUSION: There is a lack of systematic study of many female sexual dysfunctions. Orgasmic disorder and sexual pain (vaginismus and dyspaurenia) are the most extensively studied disorders and those in which sex therapy seems to have better outcomes.

Chronic Pain

View the Pain Research "Papers of the Week" from the Pain Research Forum:
http://www.painresearchforum.org/papers

Peripheral input and its importance for central sensitization.
Baron R, Hans G, Dickenson A
Ann Neurol. 2013 Sep 10. doi: 10.1002/ana.24017. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24018757

Many pain states begin with damage to tissue and/or nerves in the periphery, leading to enhanced transmitter release within the spinal cord and central sensitization. Manifestations of this central sensitization are wind-up and long-term potentiation. Hyper excitable spinal neurons show reduced thresholds, greater evoked responses, increased receptive field sizes and ongoing stimulus-independent activity; these changes probably underlie the allodynia, hyperalgesia and spontaneous pain seen in patients. Central sensitization is maintained by continuing input from the periphery, but also modulated by descending controls, both inhibitory and facilitatory, from the midbrain and brainstem. The projections of sensitized spinal neurons to the brain, in turn, alter the processing of painful messages by higher centers. Several mechanisms contribute to central sensitization. Repetitive activation of primary afferent C-fibers leads to a synaptic strengthening of nociceptive transmission. It may also induce facilitation of non-nociceptive Aβ-fibers and nociceptive Aδ-fibers, giving rise to dynamic mechanical allodynia and mechanical hyperalgesia. In post-herpetic neuralgia and complex regional pain syndrome, for example, these symptoms are maintained and modulated by peripheral nociceptive input. Diagnosing central sensitization can be particularly difficult. In addition to the medical history, quantitative sensory testing and functional magnetic resonance imaging may be useful, but diagnostic criteria which include both subjective and objective measures of central augmentation are needed. Mounting evidence indicates that treatment strategies which desensitize the peripheral and central nervous systems are required. These should generally involve a multimodal approach, so that therapies may target the peripheral drivers of central sensitization and/or the central consequences.

Chloride extrusion enhancers as novel therapeutics for neurological diseases.
Gagnon M, Bergeron MJ, Lavertu G, Castonguay A, Tripathy S, Bonin RP, Perez-Sanchez J, Boudreau D, Wang B, Dumas L, Valade I, Bachand K, Jacob-Wagner M, Tardif C, Kianicka I, Isenring P, Attardo G, Coull JA, De Koninck Y
Nat Med. 2013 Oct 6. doi: 10.1038/nm.3356. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24097188

The K^+-Cl^- cotransporter KCC2 is responsible for maintaining low Cl^- concentration in neurons of the central nervous system (CNS), which is essential for postsynaptic inhibition through $GABA_A$ and glycine receptors. Although no CNS disorders have been associated with KCC2 mutations, loss of activity of this transporter has emerged as a key mechanism underlying several neurological and psychiatric disorders, including epilepsy, motor spasticity, stress, anxiety, schizophrenia, morphine-induced hyperalgesia and chronic pain. Recent reports indicate that enhancing KCC2 activity may be the favored therapeutic strategy to restore inhibition and normal function in pathological conditions involving impaired Cl^- transport. We designed an assay for high-throughput screening that led to the identification of KCC2 activators that reduce intracellular chloride concentration ($[Cl^-]_i$). Optimization of a first-in-class arylmethylidine family of compounds resulted in a KCC2-selective analog (CLP257) that lowers $[Cl^-]_i$. CLP257 restored impaired Cl^- transport in neurons with diminished KCC2 activity. The compound rescued KCC2 plasma membrane expression, renormalized stimulus-evoked responses in spinal nociceptive pathways sensitized after nerve injury and alleviated hypersensitivity in a rat model of neuropathic pain. Oral efficacy for analgesia equivalent to that of pregabalin but without motor impairment was achievable with a CLP257 prodrug. These results validate KCC2 as a druggable target for CNS diseases.

T-type calcium channels: Functional regulation and implication in pain signaling.
Sekiguchi F, Kawabata A
J Pharmacol Sci. 2013 Aug 20;122(4):244-50.
http://www.ncbi.nlm.nih.gov/pubmed/23903007

Low-voltage-activated T-type Ca(2+) channels (T-channels), especially Cav3.2 among the three isoforms (Cav3.1, Cav3.2, and Cav3.3), are now considered to play pivotal roles in processing of pain signals. Cav3.2 T-channels are functionally modulated by extracellular substances such as hydrogen sulfide and ascorbic acid, by intracellular signaling molecules including protein kinases, and by glycosylation. Cav3.2 T-channels are abundantly expressed in both peripheral and central endings of the primary afferent neurons, regulating neuronal excitability and release of excitatory neurotransmitters such as substance P and glutamate, respectively. Functional upregulation of Cav3.2 T-channels is involved in the pathophysiology of inflammatory, neuropathic, and visceral pain. Thus, Cav3.2 T-channels are considered to serve as novel targets for development of drugs for treatment of intractable pain resistant to currently available analgesics.

Purinergic mechanisms and pain-An update.
Burnstock G
Eur J Pharmacol. 2013 Sep 15;716(1-3):24-40. doi: 10.1016/j.ejphar.2013.01.078.
http://www.ncbi.nlm.nih.gov/pubmed/23524093

There is a brief summary of the background literature about purinergic signaling. The review then considers purinergic mechanosensory transduction involved in visceral, cutaneous and musculoskeletal nociception and on the roles played by P2X3, P2X2/3, P2X4, P2X7 and $P2Y_{12}$ receptors in neuropathic and inflammatory pain. Current developments of compounds for the therapeutic treatment of both visceral and neuropathic pain are discussed.

Targeting TRP channels for pain relief.
Brederson JD, Kym PR, Szallasi A
Eur J Pharmacol. 2013 Sep 15;716(1-3):61-76. doi: 10.1016/j.ejphar.2013.03.003.
http://www.ncbi.nlm.nih.gov/pubmed/23500195

Preclinical research has recently uncovered new molecular mechanisms underlying the generation and transduction of pain, many of which represent opportunities for pharmacological intervention. Manipulating temperature-sensitive Transient Receptor Potential (TRP) channels (so-called "thermoTRPs") on nociceptive neurons is a particularly attractive strategy in that it targets the beginning of the pain pathway. In the focus of current drug development efforts are the heat-sensitive TRPV1, warm-activated TRPV3, cold-responsive TRPA1, and cool-activated TRPM8 channels. TRPV1 desensitization by topical agonists (e.g. high concentration capsaicin creams and patches) has been in clinical use for decades to alleviate chronic painful conditions like diabetic neuropathy. Currently, site-specific resiniferatoxin (an ultra potent capsaicin analogue) injections are being evaluated as "molecular scalpels" to achieve permanent analgesia in cancer patients with chronic, intractable pain. In the past few years a number of potent, small molecule TRPV1, TRPV3 and TRPA1 antagonists have been advanced into clinical trials for the treatment of inflammatory, neuropathic and visceral pain. TRPM8 antagonists are following closely behind for cold allodynia. Early TRPV1 antagonists in the clinic, however, showed worrisome adverse effects including hyperthermia and impaired noxious heat sensation. These adverse effects placed the patients at risk for scalding injury and prompted their withdrawal from the clinical trials. Second generation TRPV1 antagonists that do not cause core body temperature elevation have been reported, although the therapeutic utility of this class of compounds is not yet known. This review discusses the promise and challenges of developing TRP channel antagonists as a new generation of pain therapeutics.

Combination pharmacotherapy for management of chronic pain: From bench to bedside.
Gilron I, Jensen TS, Dickenson AH
Lancet Neurol. 2013 Sep 24. pii: S1474-4422(13)70193-5. doi: 10.1016/S1474-4422(13)70193-5. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24074723

Chronic pain, a frequently neglected problem, is treated with different classes of drugs. Current agents are limited by incomplete efficacy and dose-limiting side-effects. Knowledge of pain processing implicates multiple concurrent mechanisms of nociceptive transmission and modulation. Thus, synergistic interactions of drug combinations might provide superior analgesia and fewer side-effects than monotherapy by targeting of multiple mechanisms. Several trials in neuropathic pain, fibromyalgia, arthritis, and other disorders have assessed various two-drug combinations containing antidepressants, anticonvulsants, non-steroidal anti-inflammatories, opioids, and other agents. In some trials, combined treatment showed superiority over monotherapy, but in others improved benefit or tolerability was not seen. Escalating efforts to develop novel analgesics that surpass the efficacy of current treatments have not yet been successful; therefore, combination therapy remains an important beneficial strategy. Methodological improvements in future translational research efforts are needed to maximize the potential of combination pharmacotherapy for pain.

Advances in topical analgesics.
Anitescu M, Benzon HT, Argoff CE
Curr Opin Anaesthesiol. 2013 Aug 29. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23995062

PURPOSE OF REVIEW: The recent increase in opioid consumption in the modern world prompted pain physicians to find new and improved solutions to tackle chronic, refractory pain syndromes. Topical analgesics are emerging as a valued multimodal analgesic arm in the fight against chronic pain. RECENT FINDINGS: New and improved topical formulations have emerged as effective tools to treat chronic refractory pain. In addition to formulations manufactured by the pharmaceutical industry, there has been a recent interest in mixed topical products by local, regional and national compounding pharmacies. This review will focus on advances in topical analgesics, especially their role as an effective analgesic in nociceptive and neuropathic refractory pain states. We will explore topical analgesics' mechanisms of action and their efficacy as opioid-sparing formulations. SUMMARY: This review will allow physicians to understand the role of topical agents in the treatment of intractable pain syndromes. Increasing medical providers' familiarity with these agents will allow their incorporation as part of a complex analgesic regimen for an improved pain management plan benefiting the patient population at large.

A practical approach to prescribing antidepressants.
Shultz E, Malone DA Jr
Cleve Clin J Med. 2013 Oct;80(10):625-631.
Free full text: http://www.ccjm.org/content/80/10/625.long

Although antidepressant drugs do not differ much in their efficacy rates, the particular characteristics of one drug may make it a better choice in a given patient. This article provides insight into the art of prescribing antidepressants in primary care, with recommendations for prescribing for patients with chronic pain, sexual dysfunction, anxiety, chronic fatigue syndrome, fibromyalgia, severe insomnia, old age, diabetes, and heart problems.

Deep brain stimulation of the anterior cingulate cortex: Targeting the affective component of chronic pain.
Boccard SG, Pereira EA, Moir L, Van Hartevelt TJ, Kringelbach ML, Fitzgerald JJ, Baker IW, Green AL, Aziz TZ
Neuroreport. 2013 Oct 4. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24100411

Deep brain stimulation (DBS) has shown promise for relieving nociceptive and neuropathic symptoms of refractory chronic pain. We assessed the efficacy of a new target for the affective component of pain, the anterior cingulate cortex

(ACC). A 49-year-old man with neuropathic pain underwent bilateral ACC DBS. Patient-reported outcome measures were collected before and 2 years after surgery using a Visual Analogue Scale, Short-Form 36 quality of life survey, McGill pain questionnaire, EuroQol-5D questionnaires (EQ-5D; Health State) and neuropsychological assessments. The patient improved with DBS. Two years after surgery, the Visual Analogue Scale decreased from 6.7 to 3.0, McGill pain questionnaire improved by 42% and EQ-5D Health State increased by 150%. Stimulating the ACC at 130 Hz, 330 μs and 3 V facilitated neuropathic pain relief. The DBS remained efficacious during the 2-year follow-up period. Affective ACC DBS can relieve chronic neuropathic pain refractory to pharmacotherapy and restore quality of life.

Pain matrices and neuropathic pain matrices: A review.
Garcia-Larrea L, Peyron R
Pain. 2013 Sep 8. pii: S0304-3959(13)00494-6. doi: 10.1016/j.pain.2013.09.001. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24021862

The pain matrix is conceptualized here as a fluid system composed of several interacting networks. A nociceptive matrix receiving spinothalamic projections (mainly posterior operculoinsular areas) ensures the bodily specificity of pain and is the only one whose destruction entails selective pain deficits. Transition from cortical nociception to conscious pain relies on a second-order network, including posterior parietal, prefrontal and anterior insular areas. Second-order regions are not nociceptive-specific; focal stimulation does not evoke pain, and focal destruction does not produce analgesia, but their joint activation is necessary for conscious perception, attentional modulation and control of vegetative reactions. The ensuing pain experience can still be modified as a function of beliefs, emotions and expectations through activity of third-order areas, including the orbitofrontal and perigenual/limbic networks. The pain we remember results from continuous interaction of these subsystems, and substantial changes in the pain experience can be achieved by acting on each of them. Neuropathic pain (NP) is associated with changes in each of these levels of integration. The most robust abnormality in NP is a functional depression of thalamic activity, reversible with therapeutic manoeuvres and associated with rhythmic neural bursting. Neuropathic allodynia has been associated with enhancement of ipsilateral over contralateral insular activation and lack of reactivity in orbitofrontal/perigenual areas. Although lack of response of perigenual cortices may be an epiphenomenon of chronic pain, the enhancement of ipsilateral activity may reflect disinhibition of ipsilateral spinothalamic pathways due to depression of their contralateral counterpart. This in turn may bias perceptual networks and contribute to the subjective painful experience.

Thalamus and pain.
Yen CT, Lu PL
Acta Anaesthesiol Taiwan. 2013 Jun;51(2):73-80. doi: 10.1016/j.aat.2013.06.011. Epub 2013 Aug 2.
http://www.ncbi.nlm.nih.gov/pubmed/23968658

The thalamus is a key relay station for the transmission of nociceptive information to the cerebral cortex. We review the input-output connection, functional imaging, direct neuronal recording, stimulation, and lesioning studies on the involvement of thalamus in acute and chronic pain functions. Based on its specific reciprocal connection with the cerebral cortex, strong nociceptive responsiveness, and the severe chronic pain when it is damaged, the thalamus may hold the key to pain consciousness and the key to understanding spontaneous and evoked pain in chronic pain conditions. A work plan is proposed for future study.

Visceral sensitivity correlates with decreased regional grey matter volume in healthy volunteers: A voxel-based morphometry study.
Elsenbruch S, Schmid J, Kullmann JS, Kattoor J, Theysohn N, Forsting M, Kotsis V
Pain. 2013 Oct 4. pii: S0304-3959(13)00537-X. doi: 10.1016/j.pain.2013.09.027. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24099953

Regional changes in brain structure have been reported in patients with altered visceral sensitivity and chronic abdominal pain, such as in irritable bowel syndrome. It remains unknown if structural brain changes are associated

with visceral sensitivity. Therefore, we present the first study in healthy individuals to address whether inter-individual variations in grey matter volume (GMV) in pain-relevant regions correlate with visceral sensitivity. In 92 healthy young adults (52 females), we assessed rectal sensory and pain thresholds and performed voxel-based morphometry (VBM) to compute linear regression models with visceral sensory and pain thresholds, respectively, as independent variable and GMV in a priori-defined regions of interest (ROIs) as dependent variable. All results were family wise error (FWE) corrected at a level of $p_{FWE}<0.05$ and covaried for age. The mean (± SEM) rectal thresholds were 14.78 ± 0.46 mmHg for first sensation and 33.97 ± 1.13 mmHg for pain, without evidence of sex differences. Lower rectal sensory threshold (i.e., increased sensitivity) correlated significantly with reduced GMV in the thalamus, insula, posterior cingulate cortex, ventrolateral and orbitofrontal prefrontal cortices, amygdala and basal ganglia (all $p_{FWE}<0.05$). Lower rectal pain threshold was associated with reduced GMV in the right thalamus ($p_{FWE}=0.051$). These are the first data supporting that increased visceral sensitivity correlates with decreased grey matter volume in pain-relevant brain regions. These findings support that alterations in brain morphology do not only occur in clinical pain conditions but also according to normal inter-individual variations in visceral sensitivity.

The role of histamine in neurogenic inflammation.
Rosa AC, Fantozzi R
Br J Pharmacol. 2013 Sep;170(1):38-45. doi: 10.1111/bph.12266.
http://www.ncbi.nlm.nih.gov/pubmed/23734637

The term 'neurogenic inflammation' has been adopted to describe the local release of inflammatory mediators, such as substance P and calcitonin gene-related peptide, from neurons. Once released, these neuropeptides induce the release of histamine from adjacent mast cells. In turn, histamine evokes the release of substance P and calcitonin gene-related peptide; thus, a bidirectional link between histamine and neuropeptides in neurogenic inflammation is established. The aim of this review is to summarize the most recent findings on the role of histamine in neurogenic inflammation, with particular regard to nociceptive pain, as well as neurogenic inflammation in the skin, airways and bladder.

Gender differences in acute and chronic pain conditions: Implications for diagnosis and therapy.
[Article in German]
Schopper M, Fleckenstein J, Irnich D
Schmerz. 2013 Sep;27(5):456-466.
http://www.ncbi.nlm.nih.gov/pubmed/24026807

Gender differences can influence incidence and outcome of acute and chronic pain conditions. The reasons are to be found in genetic factors, hormonal effects and differences in anatomy and physiology. Furthermore differences relating to psychiatric comorbidities (i.e. depression) and psychosocial factors (roles, coping strategies) have been demonstrated. Men and women differ in the response to drugs and other treatments. They are differently affected by side effects of drugs. There is a gender bias in diagnosis and therapy. There is a need to study the influence of gender, age and race in order to optimize treatment towards a more individualized therapy. This article highlights already identified differences.

Sex differences in the stability of Conditioned Pain Modulation (CPM) among patients with chronic pain.
Martel MO, Wasan AD, Edwards RR
Pain Med. 2013 Aug 7. doi: 10.1111/pme.12220. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23924369

OBJECTIVES: To examine the temporal stability of conditioned pain modulation (CPM), formerly termed diffuse noxious inhibitory controls, among a sample of patients with chronic pain. The study also examined the factors that might be responsible for the stability of CPM. DESIGN, SUBJECTS, AND METHODS: In this test-retest study, patients underwent a series of standardized psychophysical pain-testing procedures designed to assess CPM on two separate occasions (i.e., baseline and follow up). Patients also completed self-report measures of catastrophizing (Pain Catastrophizing Scale [PCS] and negative affect [NA]). RESULTS: Overall, results provided evidence for the stability of CPM among patients

with chronic pain. Results, however, revealed considerable sex differences in the stability of CPM. For women, results revealed a significant test-retest correlation between baseline and follow-up CPM scores. For men, however, the test-retest correlation between baseline and follow-up CPM scores was not significant. Results of a Fisher's Z-test revealed that the stability of CPM was significantly greater for women than for men. Follow-up analyses revealed that the difference between men and women in the stability of CPM could not be accounted for by any demographic (e.g., age) and/or psychological factors (PCS and NA). CONCLUSIONS: Our findings suggest that CPM paradigms possess sufficient reliability to be incorporated into bedside clinical evaluation of patients with chronic pain, but only among women. The lack of CPM reproducibility/stability observed among men places limits on the potential use of CPM paradigms in clinical settings for the assessment of men's endogenous pain-inhibitory function.

Estrogenic influences in pain processing.
Amandusson A, Blomqvist A
Front Neuroendocrinol. 2013 Oct;34(4):329-49. doi: 10.1016/j.yfrne.2013.06.001.
http://www.ncbi.nlm.nih.gov/pubmed/23817054

Gonadal hormones not only play a pivotal role in reproductive behavior and sexual differentiation, they also contribute to thermoregulation, feeding, memory, neuronal survival, and the perception of somatosensory stimuli. Numerous studies on both animals and human subjects have also demonstrated the potential effects of gonadal hormones, such as estrogens, on pain transmission. These effects most likely involve multiple neuroanatomical circuits as well as diverse neurochemical systems and they therefore need to be evaluated specifically to determine the localization and intrinsic characteristics of the neurons engaged. The aim of this review is to summarize the morphological as well as biochemical evidence in support for gonadal hormone modulation of nociceptive processing, with particular focus on estrogens and spinal cord mechanisms.

Ethnicity and interdisciplinary pain treatment.
Gagnon CM, Matsuura JT, Smith CC, Stanos SP
Pain Pract. 2013 Jul 29. doi: 10.1111/papr.12102. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23889982

OBJECTIVE: The purpose of this study was to identify ethnic differences in interdisciplinary pain treatment outcome and whether these differences occur while controlling for the effects of demographics, psychosocial, and secondary gain. METHODS: We assessed a sample of 116 (Caucasian, African American, and Latino/a) chronic pain patients who participated a 4-week interdisciplinary pain treatment program. Outcome measure included pretreatment, post-treatment, and change scores on the Multidimensional Pain Inventory, Pain Anxiety Symptom Scale 20, Chronic Pain Acceptance Questionnaire, Coping Strategies Questionnaire-revised, and the Center for Epidemiologic Studies Depression Scale-short form. RESULTS: Analysis of covariances revealed that after accounting for educational and sex differences, ethnic minorities differed from Caucasians on a number of treatment outcome measures at pre- and post-treatment [F's ≥ 5.38; P's < 0.01]. At pretreatment, Latino/a's endorsed greater levels of pain-related anxiety, pain severity, and pain catastrophizing than Caucasians. Both Latino/a's and African Americans reported greater use of prayer at pre- and post-treatment, with Caucasians showing the greatest decrease in the use of prayer in response to treatment. At post-treatment, African Americans had higher level of depression and lower levels of reported activity than Caucasians. CONCLUSIONS: Results support the notion that ethnic differences in pain treatment outcome exist. Further, ethnic minority groups appear to have greater levels of distress compared to Caucasians. However, African Americans, Latino/a's and Caucasians demonstrated similar improvements on all outcome measures, with exception of the use of prayer. Future studies should begin to explore the mechanisms to explain why ethnic group differences in pain treatment outcome occur.

Vulvovaginal Disorders

Urogenital consequences in ageing women.
Doumouchtsis SK, Chrysanthopoulou EL
Best Pract Res Clin Obstet Gynaecol. 2013 Oct;27(5):699-714. doi: 10.1016/j.bpobgyn.2013.03.007.
http://www.ncbi.nlm.nih.gov/pubmed/23764480

Various anatomical, physiological, genetic, lifestyle and reproductive factors interact throughout a woman's life span and contribute to pelvic floor disorders. Ageing affects pelvic floor anatomy and function, which can result in a variety of disorders, such as pelvic organ prolapse, lower urinary tract symptoms, dysfunctional bowel and bladder evacuation, and sexual dysfunction. The exact mechanisms and pathophysiological processes by which ageing affects pelvic floor and lower urinary and gastrointestinal tract anatomy and function are not always clear. In most cases, it is difficult to ascertain the exact role of ageing per se as an aetiological, predisposing or contributing factor. Other conditions associated with ageing that may co-exist, such as changes in mental status, can result in different types of pelvic floor dysfunction (e.g. functional incontinence). Pelvic organ dysfunction may be associated with significant morbidity and affect quality of life. These groups of patients often pose difficult diagnostic and therapeutic dilemmas owing to complex medical conditions and concurrent morbidities. In this chapter, we summarize the current evidence on the management of pelvic floor disorders, with emphasis on elderly women and the associations between the ageing process and these disorders. Clinicians with an understanding of the affect of ageing on the pelvic floor and lower urinary and gastrointestinal tract anatomy and function, and the complex interplay of other comorbidities, will be able to investigate, diagnose and treat appropriately there women. A holistic approach may result in substantial improvements in their quality of life.

The female pelvic floor through midlife and aging.
Mannella P, Palla G, Bellini M, Simoncini T
Maturitas. 2013 Sep 6. pii: S0378-5122(13)00276-4. doi: 10.1016/j.maturitas.2013.08.008. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24055286

Female pelvic floor is a complex functional unit involved in multiple functions that extend beyond the sole support of pelvic organs. Pelvic floor dysfunction globally affects micturition, defecation and sexual activity. Evolutionary modifications such ad adaptation to upright standing, walking and the need to deliver fetuses with larger head diameters made the fascial and muscle support of the pelvic floor vulnerable, therefore predisposing women to pelvic organ prolapse and incontinence. Different than in males, the female pelvic floor undergoes a number of adaptive changes related to life and endocrine events. Most of the clinical manifestations of these changes become apparent after menopause and throughout aging in women. This review article summarizes the key aspects of the pathophysiology and the clinics of the modifications of the pelvic floor in women through midlife and beyond. A particular focus is given to the relationship between urinary and bowel dysfunction.

Practice gaps "down there": Failures in education, physical examination, recognition, diagnosis, therapy, follow-up care, and cancer surveillance in lichen sclerosus.
Margesson LJ
JAMA Dermatol. 2013 Aug 7. doi: 10.1001/jamadermatol.2013.4895. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23925700

No abstract available.

Change to either a nonandrogenic or androgenic progestin-containing oral contraceptive preparation is associated with improved sexual function in women with oral contraceptive-associated sexual dysfunction.

Davis SR, Bitzer J, Giraldi A, Palacios S, Parke S, Serrani M, Mellinger U, Nappi RE

J Sex Med. 2013 Sep 12. doi: 10.1111/jsm.12310. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24034466

INTRODUCTION: It is a commonly held belief that combined oral contraceptive (COC) pills containing an androgenic progestin may be less likely to impair sexual function than COCs containing an anti-androgenic progestin. AIM: The study aims to compare the effects of a COC containing a progestin with an anti-androgenic profile (estradiol valerate [E_2 V]/dienogest [DNG]) to that of one with an androgenic progestin (ethinyl estradiol [EE]/levonorgestrel [LNG]) on sexual function in women with COC-associated sexual dysfunction. METHODS: In this multicenter, randomized, double-blind, noninferiority study, women with COC-associated female sexual dysfunction (FSD) were randomized to E_2 V/DNG or EE/LNG for six cycles. The primary outcome was the change in the sum of Female Sexual Function Index (FSFI) desire and arousal component scores between baseline and cycle 6. Secondary outcome measures included changes to the FSFI domains, the Female Sexual Distress Scale (FSDS-R), Vaginal Health Assessment, the Atrophy Symptom Questionnaire, and the Psychological General Well Being Index over six treatment cycles. MAIN OUTCOME MEASURE: The main outcome is the change in the sum of FSFI desire and arousal component scores between baseline and cycle 6. RESULTS: Of 276 women screened, 213 received treatment and 191 completed the study. The mean increase in the sum of FSFI desire and arousal component scores was 5.90 (standard deviation [SD] 5.45) for E_2 V/DNG and 5.79 (SD 6.17) for EE/LNG (change from baseline $P < 0.0001$, both groups). Both treatments showed equal efficacy and were associated with improvements in all domains of the FSFI, with no between-group differences. Both COCs reduced the distress associated with FSD, as indicated by reduced FSDS-R scores. CONCLUSION: In women with COC-associated FSD, switching to either E_2 V/DNG or EE/LNG was associated with equivalent improvements in symptoms, challenging the perception that COCs containing anti-androgenic progestins have a detrimental effect on sexual function relative to those containing androgenic progestins.

Lichen sclerosus with vaginal involvement: Report of 2 cases and review of the literature.

Zendell K, Edwards L

JAMA Dermatol. 2013 Aug 7. doi: 10.1001/jamadermatol.2013.4885. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23925660

IMPORTANCE Lichen sclerosus (LS) is an uncommon chronic inflammatory disease that most commonly affects anogenital skin of postmenopausal women. It typically manifests as atrophic white plaques, which may be accompanied by purpura or fissuring. Rarely, LS has been observed to affect mucosal tissues in the mouth and the penile urethra. It is generally taught that LS does not affect the vagina, unlike lichen planus. To our knowledge, only one case report of LS with vaginal involvement exists in the literature. OBSERVATIONS Two cases of severe vulvar LS with vaginal involvement are reported. Both cases exhibited characteristic features of LS on vaginal biopsy, and both patients were followed up clinically without further treatment of the vagina. CONCLUSIONS AND RELEVANCE Vaginal LS may be more common than previously thought and may be underdiagnosed. Patients with more severe disease or with significant vaginal atrophy may be more likely to have involvement of the vagina. In addition, patients with pelvic organ laxity may be at increased risk if their vaginal walls are chronically exposed because of prolapse. Physicians managing patients withvulvar LS should be aware of the possibility of vaginal involvement so that vaginal lesions may be diagnosed and followed up appropriately.

Clotrimazole dampens vaginal inflammation and neutrophil infiltration in response to Candida Albicans infection.
Wilson D, Hebecker B, Moyes DL, Miramón P, Jablonowski N, Wisgott S, Allert S, Naglik JR, Hube B
Antimicrob Agents Chemother. 2013 Oct;57(10):5178-80. doi: 10.1128/AAC.01244-13.
http://www.ncbi.nlm.nih.gov/pubmed/23896471

The pathology of vulvovaginal candidiasis (VVC) caused by Candida albicans is associated with a non-protective inflammatory response and is frequently treated with clotrimazole. We investigated the mechanisms by which clotrimazole resolves VVC. Low levels of clotrimazole, which do not block fungal growth, inhibit expression of a "danger response" transcription factor, c-Fos, block production of pro-inflammatory cytokines, and inhibit neutrophil infiltration to the site of infection.

Bazedoxifene + conjugated estrogens in HT for the prevention of osteoporosis and treatment of vasomotor symptoms associated with the menopause.
Tella SH, Gallagher JC
Expert Opin Pharmacother. 2013 Oct 7. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24093499

Introduction: The recent concept that estrogen agonist-antagonists, often referred to as selective estrogen receptor modulators, can be combined with an estrogen has led to the development of a novel form of menopausal therapy called Tissue-Selective Estrogen Complex (TSEC). This paper reviews the TSEC bazedoxifene and conjugated equine estrogens (BZA/CE). Areas covered: This review is based on clinical trials and a PubMed search. The pharmacokinetics and pharmacodynamics of BZA in BZA plus CE are reviewed. This review outlines the effects of this particular TSEC, which maintains or increases bone mineral density in women at high risk for osteoporosis, and has clinical qualities of a promising new menopausal therapy. The potential adverse effects of BZA/CE combinations are summarized. Expert opinion: A TSEC that contains CE and BZA that has both estrogen agonist and antagonist effects has reached clinical development. Phase III clinical trials show this TSEC relieves hot flashes, improves vulvo-vaginal atrophy and its symptoms, does not stimulate the endometrium, and prevents bone loss. In the trials so far it appears to have a good safety and tolerability profile. The optimum combination of BZA/CE combination is 20 mg BZA with CE 0.45 and 0.625 mg daily.

Tissue selectivity of ospemifene: Pharmacologic profile and clinical implications.
Kangas L, Unkila M
Steroids. 2013 Sep 18. pii: S0039-128X(13)00199-2. doi: 10.1016/j.steroids.2013.09.003. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24055829

The multifactorial consequences of menopausal estrogen deficiency affect numerous tissues throughout the body. Supplemental hormonal therapies carry the burden of a risk/benefit ratio that must be highly individualized. Selective estrogen receptor modulators (SERMs) are estrogen receptor (ER) agonist/antagonists designed to induce benefits comparable with estrogen while minimizing adverse effects. Here, we review the estrogen agonist/antagonist profile of ospemifene, a novel triphenylethylene derivative recently approved to treat dyspareunia, a symptom of vulvar and vaginal atrophy (VVA) due to menopause, both pre-clinically and clinically. Ospemifene binds ERα and ERβ with approximately equal affinities. In preclinical models, ospemifene increased vaginal and uterine epithelial thickness and mucification to the same extent as estrogen. Ospemifene did not induce endometrial hyperplasia in animal models; there also was no stimulatory effect on endometrial cells. In rat and human mammary cells in vitro, ospemifene evokes a dose-dependent inhibition on estrogen-induced cell responses and cell proliferation, supporting an anti-estrogenic effect in breast. In contrast, ospemifene has an estrogenic effect on bone, as seen by improved bone mineral density, strength, mass, and histomorphometry in preclinical models, consistent with improvements in markers of bone resorption and formation in postmenopausal women. Based on the preclinical evidence, ospemifene has beneficial estrogen-like effects on the vaginal epithelium, preliminary evidence to support a neutral endometrial profile, anti-proliferative effects in breast, and estrogenic effects in bone. Taken together, especially regarding estrogen-like effects

on the vaginal epithelium, ospemifene presents a profile of tissue-specific effects that appear novel among available SERMs and well-suited for the treatment of VVA.

Promestriene, a specific topic estrogen. Review of 40 years of vaginal atrophy treatment: Is it safe even in cancer patients?
Del Pup L, Di Francia R, Cavaliere C, Facchini G, Giorda G, De Paoli P, Berretta M
Anticancer Drugs. 2013 Nov;24(10):989-998.
http://www.ncbi.nlm.nih.gov/pubmed/24080714

Urogenital symptoms resulting from estrogen deficiency are common problems that impair quality of life and sexuality. Potentially, one out of three postmenopausal women could benefit from a vaginal estrogen therapy, but the fear of systemic absorption limits its use. Promestriene used vaginally to relieve vaginal atrophy is a locally effective estrogen that has not shown systemic estrogenic effects. Thus, it could be a first-line option for those who necessitate a minimal or ideally no vaginal absorption, particularly in symptomatic cancer patients. There are little data available in the literature, mostly consisting of small, open-label, short duration studies, and few randomized-controlled studies. After a long-term market experience (almost 40 years), in 34 countries, and millions of pieces prescribed, the side effects were very rarely reported in pharmacovigilance data, whereas the effectiveness to relieve atrophy was good. To further improve promestriene safety, especially in estrogen-sensitive cancer patients, a very low dose is used from the beginning, starting from half or less of the usual dose, and then gradually increased till the minimum effective dose, which could further reduce its already minimal vaginal absorption.

Aromatase inhibitors affect vaginal proliferation and steroid hormone receptors.
Kallak TK, Baumgart J, Göransson E, Nilsson K, Poromaa IS, Stavreus-Evers A
Menopause. 2013 Sep 30. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24080848

OBJECTIVE: Women with breast cancer who are treated with aromatase inhibitors often experience vaginal atrophy symptoms and sexual dysfunction. This work aims to study proliferation and the presence and distribution of steroid hormone receptors in vaginal biopsies in relation to vaginal atrophy and vaginal pH in women with breast cancer who are on adjuvant endocrine treatment and in healthy postmenopausal women. METHODS: This is a cross-sectional study that compares postmenopausal aromatase inhibitor-treated women with breast cancer (n = 15) with tamoxifen-treated women with breast cancer (n = 16) and age-matched postmenopausal women without treatment (n = 19) or with vaginal estrogen therapy (n = 16). Immunohistochemistry was used to study proliferation and steroid hormone receptor staining intensity. Data was correlated with estrogen and androgen levels, vaginal atrophy scores, and vaginal pH. RESULTS: Aromatase inhibitor-treated women had a lower grade of proliferation, weaker progesterone receptor staining, and stronger androgen receptor staining, which correlated with plasma estrone levels, vaginal atrophy scores, and vaginal pH. CONCLUSIONS: Women with aromatase inhibitor-treated breast cancer exhibit reduced proliferation and altered steroid hormone receptor staining intensity in the vagina, which are related to clinical signs of vaginal atrophy. Although these effects are most probably attributable to estrogen suppression, a possible local inhibition of aromatase cannot be ruled out.

Attitudes and approaches to vaginal atrophy in postmenopausal women: A focus group qualitative study.
Utian WH, Maamari R
Climacteric. 2013 Oct 1. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24083795

ABSTRACT Objective: The impact of postmenopausal vaginal atrophy and women's coping strategies were evaluated through international focus groups. Methods: Three-hour focus groups of 3-5 postmenopausal women who had symptoms of vaginal atrophy but had not sought treatment were conducted in Canada, Sweden, the United States, and the United Kingdom. Participants were asked about their experience with menopause and vaginal atrophy, including use

of nonprescription treatments and their interactions with health care providers. Women were classified as one of 5 personality types, based on their interaction with the world (individualism or belonging) and strategies for coping with stress (control or liberation). Results: Vaginal atrophy was not recognized as a medical condition by focus group participants, and women had not used treatments for vaginal atrophy apart from nonprescription lubricants. Women who had discussed vaginal atrophy symptoms with their doctor felt their concerns were dismissed as a normal part of aging, and they did not receive counseling about treatment options such as low-dose estrogen therapy. Those whose coping strategy involved dominance, combating or individualism were more likely to seek treatment than those whose strategy involved submission, acceptance or belonging. Women who used control to cope with menopausal changes were more likely to respond to information validated by perceived experts than were those who used a strategy of release. Conclusions: Women's reactions to their vaginal atrophy varied according to personality. Use of a personality-based approach to patient counseling may encourage patients to discuss vaginal atrophy with their health care provider and seek treatment.

Atopy, the barrier, urine and genital lichen sclerosus.
Becker K
Br J Dermatol. 2013 Aug 2. doi: 10.1111/bjd.12554. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23909607

We thank Dr. Bunker for adding another condition playing a role in the pathogenesis of LS. Indeed the "warm, moist, urine-exposed environment" was postulated as predilecting BXO in the observation of Depasquale and al. (1) We refer to this theory in our review of 225 cases of LS in boys. (2) We could confirm the observation of recurrence of LS after circumcision in a boy whose obesity had led to a pseudoprepuce caused by the phenomenon of buried penis. So exposure to urine is probably a factor. There are a lot of studies and data in literature indicating a relationship between autoimmunity and LS.

Short-term surgical outcomes and characteristics of patients with mesh complications from pelvic organ prolapse and stress urinary incontinence surgery.
Hammett J, Peters A, Trowbridge E, Hullfish K
Int Urogynecol J. 2013 Oct 2. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24085144

INTRODUCTION AND HYPOTHESIS: Surgical treatment of pelvic organ prolapse (POP) and stress urinary incontinence (SUI) can include the use of synthetic materials. Placement of synthetic materials into the vaginal wall, through either the vagina or the abdomen, includes the risk of complications such as vaginal wall extrusion or pain. There is little data regarding outcomes following treatment of mesh complications. METHODS: A retrospective chart review of patients who underwent excision of mesh placed for POP or SUI between 1 January 2001 and 31 October 2012 was performed at the University of Virginia. Chart abstraction queried patient demographics, clinical history, physical examination, pre- and post-excision symptoms, and operative findings. The International Continence Society (ICS) and International Urogynecological Association (IUGA) classification system was used to define the nature and location of mesh complications. RESULTS: A total of 57 patients (26 mid-urethral slings, 23 transvaginal prolapse, 9 intraperitoneal prolapse) with the diagnosis of mesh extrusion into the vaginal wall were analyzed. Twenty-five (average 2.8 cases/year) original mesh surgeries occurred between January 2001 and January 2010 and 41 (average 20.5 cases/year) occurred after January 2010. The most common presenting patient complaints were chronic pelvic pain (55.9 %), dyspareunia (54.4 %), and vaginal discharge (30.9 %). At a 6-week post-operative visit, 57.3 % of patient's symptoms were completely resolved and 14.6 % were improved. CONCLUSION: Clinicians should be cognizant of the variable presentations of post-operative vaginal mesh complications. Mesh excision by experienced pelvic surgeons is an effective and safe treatment for these complications; however, a significant number of patients may have persistent symptoms following surgery.

Evaluation of the activity and safety of CS 21 Barrier Genital Gel® compared to topical aciclovir and placebo in symptoms of genital herpes recurrences: A randomized clinical trial.

Khemis A, Duteil L, Tillet Y, Dereure O, Ortonne JP

J Eur Acad Dermatol Venereol. 2013 Sep 7. doi: 10.1111/jdv.12228. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/24010876

BACKGROUND: Topical or systemic antiviral drugs reduce the duration of genital herpes recurrences but may not always alleviate functional symptoms. OBJECTIVES: To assess the efficacy and safety of oxygenated glycerol triesters-based CS21 barrier genital gel® vs. topical aciclovir and placebo (vehicle) in resolving functional symptoms and in healing of genital herpes recurrences. METHODS: A prospective randomized controlled, investigator-blinded trial of CS21 barrier genital gel® vs. topical aciclovir (reference treatment) and placebo (vehicle) was designed. The primary endpoint was the cumulative score of four herpes-related functional symptoms (pain, burning, itching and tingling sensations). Secondary endpoints included objective skin changes (erythema, papules, vesicles, oedema, erosion/ulceration, crusts), time to heal, local tolerance and overall acceptability of the treatment as reported by a self-administered questionnaire. RESULTS: Overall, 61 patients were included. CS 21 barrier genital gel® was significantly more efficient than topical aciclovir and vehicle for subjective symptoms and pain relief in genital herpes recurrences; additionally, time to heal was significantly shorter with CS 21 than with vehicle, whereas no significantly difference was observed between patients receiving topical aciclovir and vehicle. The treatments under investigation were well tolerated and the adverse events were comparable in the three treatment groups. CONCLUSION: Overall, these results support the interest of using of CS 21 barrier genital gel® in symptomatic genital herpes recurrences. Accordingly, this product offers a valuable alternative in topical management of recurrent genital herpes.

Ethinylestradiol is beneficial for postmenopausal patients with heavily pre-treated metastatic breast cancer after prior aromatase inhibitor treatment: a prospective study.

Iwase H, Yamamoto Y, Yamamoto-Ibusuki M, Murakami KI, Okumura Y, Tomita S, Inao T, Honda Y, Omoto Y, Iyama KI

Br J Cancer. 2013 Sep 17;109(6):1537-42. doi: 10.1038/bjc.2013.520.

http://www.ncbi.nlm.nih.gov/pubmed/24002591

Background: Oestrogens usually stimulate the progression of oestrogen receptor (ER)-positive breast cancer. Paradoxically, high-dose oestrogens suppress the growth of these tumors in certain circumstances. Methods: We prospectively examined the efficacy and safety of ethinylestradiol treatment (3 mg per day oral) in postmenopausal patients with advanced or recurrent ER-positive breast cancer who had previously received endocrine therapies, especially those with resistance to aromatase inhibitors. Results: Eighteen patients were enrolled with the median age of 63 years and the mean observation time of 9.2 months. Three cases withdrew within 1 week due to oestrogen flare reactions with nausea, fatigue and muscle-skeletal pain. The response rate was 50% (9 out of 18), and the clinical benefit rate was 56% (10 out of 18). The stable disease (<6 months) was 17% (3 out of 18) and another 2 cases were judged as progressive disease. Time-to-treatment failure including 2 on treatment was a median of 5.6 months (range 0.1 to 14.5(+)). Although vaginal bleeding or endometrial thickening was observed in patients receiving long-term treatment, there were no severe adverse events, such as deep venous thrombosis or other malignancies. Conclusion: Although the mechanism of this treatment has not been fully understood, our data may contribute to change the common view of late-stage endocrine therapy.

The impact of pelvic floor surgery on female sexual function: A mixed quantitative and qualitative study.

Roos A, Thakar R, Sultan A, de Leeuw J, Paulus A

BJOG. 2013 Sep 10. doi: 10.1111/1471-0528.12412. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/24020923

OBJECTIVE: To assess whether the current condition-specific sexual function questionnaire provides full insight into sexual function following pelvic floor surgery. DESIGN: Prospective, mixed quantitative and qualitative study. SETTING: Urogynaecology clinic in a large university hospital. POPULATION: Thirty-seven women undergoing surgery for pelvic organ prolapse (POP) and/or stress urinary incontinence (SUI). METHODS: Women were seen before surgery and

3 months postoperatively. At both visits the Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ) was completed and a qualitative face-to-face semi-structured interview was conducted. PISQ total and domain scores, as well as the change in the preoperative and postoperative score, were calculated and analyzed using Wilcoxon signed rank test and one-sample t-test. The qualitative data were systematically analyzed using data-matrices. MAIN OUTCOME MEASURES: The impact of pelvic floor surgery on female sexual function. RESULTS: Significant improvement was seen for PISQ total score (P = 0.003) as well as Physical (P < 0.001) and Partner-related (P = 0.002) domains, but not for the Behavioral/Emotive domain (P = 0.220). Analysis of qualitative data showed that improvement in sexual function was a result of cure of POP and SUI symptoms. Deterioration of sexual function was due to dyspareunia, fear of causing damage to the surgical result, new symptoms and a disappointing result of surgery. CONCLUSIONS: Our qualitative data show that PISQ is limited in the assessment of sexual function after pelvic floor surgery as it does not assess most surgery-specific negative effects on sexual function.

Single-dose and steady-state pharmacokinetics of ospemifene, a selective estrogen receptor modulator, in postmenopausal women.
Koskimies P, Turunen J, Lammintausta R, Scheinin M
Int J Clin Pharmacol Ther. 2013 Sep 30. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24075094

Objective: To characterize the pharmacokinetics of the oral, non-estrogen agent ospemifene, an estrogen agonist/antagonist with tissue-selective effects (also called a selective estrogen receptor modulator) that was recently approved for the treatment of dyspareunia associated with vulvar and vaginal atrophy in postmenopausal women. Methods: Two open-label, Phase 1 studies were conducted to determine the pharmacokinetics of ospemifene in healthy postmenopausal women. In the single-dose study, 60 mg of [3H]-ospemifene was orally administered to 6 subjects. Blood, urine, and fecal samples were collected pre-dose and serially up to 240 hours post-dose. In the multiple-dose study, 12 subjects received 60 mg of ospemifene once daily for 9 days. Blood samples were collected pre-dose and serially post-dose on Day 1, pre-dose on Days 7 and 8, and pre-dose and serially post-dose on Day 9. Results: Ospemifene exhibited high plasma protein binding and was extensively metabolized, predominantly to 4-hydroxyospemifene and 4'-hydroxyospemifene. In the single-dose study, ospemifene was rapidly absorbed, with a median tmax of 1.50 hours and geometric mean Cmax of 612 ng/ml. The geometric mean (CV%) t1/2 was 24.5 (21.3) hours and 29.0 (18.0) hours for ospemifene and 4-hydroxyospemifene, respectively. Fecal elimination accounted for 75% of the administered [3H]-ospemifene dose in 240 hours. In the multiple dosing study, steady state was reached by Day 7. The mean t1/2 at steady state for ospemifene was 29.1 hours. High values for volume of distribution and total clearance suggested extensive tissue distribution and efficient elimination of ospemifene. Conclusions: In healthy postmenopausal women, ospemifene 60 mg/day reached steady state concentrations by Day 7 and showed minimal accumulation of parent drug or its two main metabolites, indicating that once daily dosing is appropriate.

Isolated, localised extragenital bullous lichen sclerosus et atrophicus: A rare entity.
Khatu S, Vasani R
Indian J Dermatol. 2013 Sep;58(5):409.
Free full text: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3778813/

Lichen sclerosus et atrophicus (LSA) is a rare, chronic, mucocutaneous disease of unknown cause. Onset can occur in subjects of any age but more prevalent in adult females around the time of menopause. In both the sexes ano-genital involvement is more common. Extra-genital cases are rare, and common localizations are neck and shoulders, axilla, upper arms, flexor aspects of wrists and around the umbilicus. Bullous LSA is an unusual manifestation of the disease. Isolated extra-genital bullous LSA is a distinctly rare event with very few cases reported till date.

Severe gynecologic sequelae of stevens-johnson syndrome and toxic epidermal necrolysis caused by ibuprofen: A case report.

Pliskow S

J Reprod Med. 2013 Jul-Aug;58(7-8):354-6.
http://www.ncbi.nlm.nih.gov/pubmed/23947089

BACKGROUND: Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a serious, drug-induced, life-threatening condition characterized by an epidermal blistering rash with necrosis, desquamation and mucosal surface involvement. This patient represents the youngest and most significant case report in the literature of gynecologic damage due to TEN. CASE: A 31/2-year-old girl developed TEN involving 90% of her body surface area after exposure to pediatric ibuprofen. After onset of puberty she required surgery to treat vulvar, vaginal and cervical adhesions, stenosis and hematometra. CONCLUSION: While delaying evaluation and treatment of the extremely young child with this disorder until puberty has been the standard, consideration should be given to earlier evaluation and intervention.

Update on the classification and treatment of localized scleroderma.

Bielsa Marsol I

Actas Dermosifiliogr. 2013 Oct;104(8):654-66. doi: 10.1016/j.adengl.2012.10.012.
Free full text: http://www.actasdermo.org/en/update-on-the-classification-and/articulo/90229899/?pubmed=true

Morphea or localized scleroderma is a distinctive inflammatory disease that leads to sclerosis of the skin and subcutaneous tissues. It comprises a number of subtypes differentiated according to their clinical presentation and the structure of the skin and underlying tissues involved in the fibrotic process. However, classification is difficult because the boundaries between the different types of morphea are blurred and different entities frequently overlap. The main subtypes are plaque morphea, linear scleroderma, generalized morphea, and pansclerotic morphea. With certain exceptions, the disorder does not have serious systemic repercussions, but it can cause considerable morbidity. In the case of lesions affecting the head, neurological and ocular complications may occur. There is no really effective and universal treatment so it is important to make a correct assessment of the extent and severity of the disease before deciding on a treatment approach.

The use of argon beam coagulation in treating vulvar intraepithelial neoplasia III: A retrospective review.

Kushnir CL, Fleury AC, Hill MC, Silver DF, Spirtos NM

Gynecol Oncol. 2013 Jul 23. pii: S0090-8258(13)00839-1. doi: 10.1016/j.ygyno.2013.06.006. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23887037

Argon beam coagulation (ABC) has unique properties which make it suitable for the local treatment of superficial epithelial disorders such as vulvar intraepithelial neoplasia (VIN III). OBJECTIVE: To evaluate argon beam coagulation in treating multifocal VIN III. METHODS: Argon beam coagulation was used in twenty-nine patients. ABC was set at 80W, 7L/min. All patients were given 1% silvadene cream to apply to vulva. Patients had follow-up appointments two weeks and six weeks postoperatively. Patients were followed every three to six months for the subsequent year. RESULTS: 2 of 29 (6.8%) experienced moderate pain within the first two weeks postoperatively requiring prescriptions for perocet. 2 of 29 (6.8%) had yeast infection requiring diflucan. Mean follow-up time was 34.9months (11.7-37.4). 15 of 29 (51.7%) had no recurrence within the follow-up period. 14 of 29 (48.3%) recurred within the follow-up period. The mean time to recurrence is 23.2months. CONCLUSION: This small retrospective review is the first to evaluate argon beam coagulation in treating multifocal VIN III. This review indicates that ABC is comparable to other vulva organ conserving therapies. ABC retains cosmesis, and form of the vulva. This is a major advantage over surgery. Repeat treatments are also possible, which is important in a condition such as VIN, which tends to be multifocal and recurrent.

Increased osteopontin expression is associated with progression from vulvar precancerous lesions to vulvar squamous cell carcinoma.
Wu Z, Shen Y, Gong K, Wu Z, Zhang T, Zhang X, Li S
Arch Gynecol Obstet. 2013 Aug 25. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23978873

PURPOSE: Vulvar squamous cell carcinoma (VSCC) contributes to about 3-5 % of all gynecological cancers. Vulvar intraepithelial neoplasia (VIN) and vulvar lichen sclerosus (VLS) are regarded as precancerous lesions. Early detection and treatment of precancerous lesions may prevent development of VSCC. Osteopontin (OPN) has been shown to be involved in many physiological and pathological processes, such as tumor progression, by promoting cancer cell invasion and metastasis. As a result of these findings, OPN has been described as a potential marker for tumor progression in some malignancies. In this study, we investigated the expression of OPN in vulvar tissue specimens and compared its expression between different histopathological grades. METHODS: In the present study, the expression patterns of OPN in 80 paraffin-embedded tissue specimens, including 25 VSCC samples, 21 VIN lesions and 21 VLS, in addition to 13 normal vulvar samples, were examined by the immunohistochemical method and chromogenic in situ hybridization. RESULTS: The intensity of OPN expression steadily increased according to the pathological grades. In addition, OPN staining was found in the extracellular matrix in VSCC. CONCLUSIONS: Expression levels of OPN increased from VLS and VIN to VSCC, and steadily increased with the pathological stage of VSCC. Our results suggest that OPN may be associated with the progression of VSCC.

Electrochemotherapy can be used as palliative treatment in patients with repeated loco-regional recurrence of squamous vulvar cancer: A preliminary study.
Perrone AM, Galuppi A, Cima S, Pozzati F, Arcelli A, Cortesi A, Procaccini M, Pellegrini A, Zamagni C, De Iaco P
Gynecol Oncol. 2013 Sep;130(3):550-3. doi: 10.1016/j.ygyno.2013.06.028.
http://www.ncbi.nlm.nih.gov/pubmed/23811116

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

Vaginismus and our experience in treating this sexual problem.
[Article in Bulgarian]
Sirakov M
Akush Ginekol (Sofiia). 2013;52(1):61-6.
http://www.ncbi.nlm.nih.gov/pubmed/23805463

According to various statistics from 4.2 to 42% of women in reproductive age, complained of a mild or severe problems in sexual function. The study presents own data on treatment of vaginismus in 14 girls and young women aged 16 to 36 years who have turned from 2007 to 2012 to the Cabinet Children and adolescent gynaecology at the University Hospital

"Maychin dom". A primary examination established a high and tenacious hymen in 7 (50%) patients. The patients demonstrated fear, but still allowed careful examination. At 3 girls (21.43%) a combined cause of complaints was found. They demonstrated fear of pain during coitus and reported bad memory of the first sexual attempts; they had high and tenacious hymen and were able to tolerate touching the vulva after much persusions. In 3 (21.43%) patients consequences of puritan education were registered. They did not allowed to touch the vulva despite the declaration that would allow such. In one patients (7.14%) a un-stretchable vagina was found. She demonstrated dyspareunia (avoiding intercourse and having one failed marriage) but she tolerated penetration of her vagina of one phalanx. In all cases of vaginismus we performed educational lectures and artefitial defloration.

Vulvar and vaginal atrophy in postmenopausal women: Findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) Survey.
Kingsberg SA, Wysocki S, Magnus L, Krychman ML
J Sex Med. 2013 Jul;10(7):1790-9. doi: 10.1111/jsm.12190.
http://www.ncbi.nlm.nih.gov/pubmed/23679050

INTRODUCTION: Vulvar and vaginal atrophy (VVA) is a chronic medical condition experienced by many postmenopausal women. Symptoms include dyspareunia (pain with intercourse), vaginal dryness, and irritation and may affect sexual activities, relationships, and activities of daily life. AIM: The aim of this study is to characterize postmenopausal women's experience with and perception of VVA symptoms, interactions with healthcare professionals (HCPs), and available treatment options. METHODS: An online survey was conducted in the United States in women from Knowledge Panel (®) , a 56,000-member probability-selected Internet panel projectable to the overall US population. Altogether, 3,046 postmenopausal women with VVA symptoms (the largest US cohort of recent surveys) responded to questions about their knowledge of VVA, impact of symptoms on their activities, communication with HCPs, and use of available treatments. MAIN OUTCOME MEASURES: Percent is calculated as the ratio of response over total responding for each question for all and stratified participants. RESULTS: The most common VVA symptoms were dryness (55% of participants), dyspareunia (44%), and irritation (37%). VVA symptoms affected enjoyment of sex in 59% of participants. Additionally, interference with sleep, general enjoyment of life, and temperament were reported by 24%, 23%, and 23% of participants, respectively. Few women attributed symptoms to menopause (24%) or hormonal changes (12%). Of all participants, 56% had ever discussed VVA symptoms with an HCP and 40% currently used VVA-specific topical treatments (vaginal over-the-counter [OTC] products [29%] and vaginal prescription therapies [11%]). Of those who had discussed symptoms with an HCP, 62% used OTC products. Insufficient symptom relief and inconvenience were cited as major limitations of OTC products and concerns about side effects and cancer risk limited use of topical vaginal prescription therapies. CONCLUSIONS: VVA symptoms are common in postmenopausal women. Significant barriers to treatment include lack of knowledge about VVA, reluctance to discuss symptoms with HCPs, safety concerns, inconvenience, and inadequate symptom relief from available treatments.

Diagnostic criteria for erosive lichen planus affecting the vulva: An international electronic-delphi consensus exercise.
Simpson RC, Thomas KS, Leighton P, Murphy R
Br J Dermatol. 2013 Aug;169(2):337-43. doi: 10.1111/bjd.12334.
http://www.ncbi.nlm.nih.gov/pubmed/23521206

BACKGROUND: There is no defined set of criteria for diagnosing erosive lichen planus affecting the vulva (ELPV) and there is geographical variation in management. OBJECTIVES: To reach consensus on clinicopathological diagnostic criteria for ELPV. METHODS: This was a three-stage international electronic-Delphi exercise with a subsequent formal feedback process. In the first two rounds participants were asked to rate the importance of a list of clinicopathological criteria. Responses from round 1 were summarized and presented in round 2, along with additional criteria suggested by participants. In round 3, participants were asked to rate the items that had reached consensus as 'essential' or 'supportive' features in diagnosing ELPV. Consensus was defined as being reached if 75% of participants agreed on the importance of an item. RESULTS: A total of 73 experts representing dermatology, gynaecology, histopathology and genitourinary medicine participated; 69 (95%) completed all three rounds. Consensus was achieved for the following 'supportive' diagnostic criteria: (i) well-demarcated erosions/erythematous areas at the vaginal introitus; (ii) presence of

a hyperkeratotic border to lesions and/or Wickham striae in surrounding skin; (iii) symptoms of pain/burning; (iv) scarring/loss of normal architecture; (v) presence of vaginal inflammation; (vi) involvement of other mucosal surfaces; (vii) presence of a well-defined inflammatory band involving the dermoepidermo junction; (viii) presence of an inflammatory band consisting predominantly of lymphocytes; and (ix) signs of basal layer degeneration. It was suggested that at least three supportive features should be present to make a diagnosis of ELPV, although this number is subject to further discussion. CONCLUSIONS: This study has identified a diagnostic dataset for ELPV that can be adopted into clinical practice and clinical trials.

Mycoplasma pneumoniae: A rare cause of vulvar ulcers or an undiagnosed one?
Vieira-Baptista P, Machado L, Costa AR, Beires J, Martinez-de-Oliveira J
J Low Genit Tract Dis. 2013 Jul;17(3):330-4. doi: 10.1097/LGT.0b013e3182710896.
http://www.ncbi.nlm.nih.gov/pubmed/23486069

OBJECTIVES: Acute vulvar ulcers are quite common, and often, an etiological diagnosis cannot be achieved. This article reports 3 cases of vulvar ulcers in adult women infected with Mycoplasma pneumoniae. The authors were able to find only one similar report in the literature. MATERIAL AND METHODS: Two women in their third decade of life and 1 in the fourth presented to the hospital with acute and intense vulvar pain. Two of them reported oropharyngeal symptoms in the preceding days. All 3 presented with extensive, painful, and destructive vulvar ulcers. A standard protocol was applied, including samples taken from the ulcer (microbiology and polymerase chain reaction) and blood drawn for serological examination and liver function testing. All 3 had the remarkable finding of a positive immunoglobulin G (IgG) and IgM for M. pneumonia (in one of the cases, IgM was initially inconclusive but turned to positive when repeated 2 weeks later). One patient had an extensive destruction of one labium minus, requiring surgical reconstruction. RESULTS: Two of them were treated with antibiotics, and one was not. However, in fact, all 3 healed in a similar period, making it probable that this kind of medication is not helpful. CONCLUSIONS: M. pneumoniae might be associated with some cases of vulvar ulcers and should always be tested in this context. Probably, antibiotic treatment is not helpful, even when this agent is identified as the possible causal agent of vulvar ulcers.

Labial fusion causing recurrent cyst formation and a novel approach to surgical management.
Selco MM, Doss RH, Gruber DD, Shippey SH
Female Pelvic Med Reconstr Surg. 2013 Sep-Oct;19(5):312-4. doi: 10.1097/SPV.0b013e318292460e.
http://www.ncbi.nlm.nih.gov/pubmed/23982585

BACKGROUND: Labial fusion may occur as a result of lichen sclerosus, lichen planus, genital mutilation, obstetric laceration, and atrophic vaginitis. Koebner phenomenon, or reformation of scar tissue over the clitoris after trauma to the involved tissue, may confound attempts at surgical management. CASE: A 22-year-old nulligravid patient presented with labia minora fusion that had been present since childhood. Her most bothersome symptoms were the recurrence of periclitoral pseudocysts with pain and discharge after spontaneous or needle drainage. Her symptoms and examination findings persisted despite a prolonged course of topical clobetasol, and she desired surgical intervention. A silastic vessel loop was placed through the tract between her clitoris and fused overlying labia. The ends of the vessel loop were brought together and tied in a fashion similar to cutting setons used to manage complex anal fistulae. Over the subsequent weeks, additional ties were used to sequentially tighten the loop and gradually divide the fused labia, ultimately exposing the patient's normal clitoris, which was uninjured by the procedure. Topical clobetasol was used throughout the process to prevent reagglutination of the labia. CONCLUSIONS: Our experience suggests that adaptation of a cutting seton may be used effectively in the surgical management of labial fusion to allow for gradual division of the skin bridge while minimizing the risk of recurrence of agglutination.

Two case presentations of profound labial edema as a presenting symptom of Hypermobility-Type Ehlers-Danlos Syndrome.

Krapf JM, Goldstein AT

J Sex Med. 2013 Sep;10(9):2347-50. doi: 10.1111/jsm.12229.

http://www.ncbi.nlm.nih.gov/pubmed/23875629

INTRODUCTION: Hypermobility-type Ehlers-Danlos syndrome (EDS), an often-missed diagnosis with the potential for serious sequelae, may have a variety of uncommon presentations, some of which may be gynecologic. AIM: The aim of this case report is to present two cases of profound labial edema associated with intercourse as a presenting symptom of hypermobility-type EDS. METHODS: A 25-year-old female presented with severe labia minora swelling and bladder pressure associated with intercourse, in addition to persistent genital arousal. History revealed easy bruising, joint pain, and family history of aneurysm. A 22-year-old female presented with intermittent profound labial swelling for 6 years, associated with sensitivity and pain with intercourse. The patient has a history of joint pain and easy bruising, as well a sister with joint hypermobility and unexplained lymphedema. The presenting symptom of profound labial edema led to the diagnosis of hypermobility-type EDS. RESULTS: Patients with hypermobility syndrome exhibit an increased ratio of type III collagen to type I collagen, causing tissue laxity and venous insufficiency. Abnormal collagen may lead to gynecologic manifestations, including unexplained profound labial edema, pelvic organ prolapse in the absence of risk factors, and possibly persistent genital arousal. CONCLUSIONS: This case report highlights the need for further research to determine incidence of labial edema in hypermobility-type EDS and to further elucidate a potential correlation between profound labial edema and collagen disorders. Krapf JM and Goldstein AT. Two case presentations of profound labial edema as a presenting symptom of hypermobility-type Ehlers-Danlos syndrome. J Sex Med 2013;10:2347-2350.

Body image and genital self-image in pre-menopausal women with dyspareunia.

Pazmany E, Bergeron S, Van Oudenhove L, Verhaeghe J, Enzlin P

Arch Sex Behav. 2013 Aug;42(6):999-1010. doi: 10.1007/s10508-013-0102-4.

http://www.ncbi.nlm.nih.gov/pubmed/23605571

With a prevalence of 15-21%, dyspareunia is one of the most commonly reported sexual dysfunctions in pre-menopausal women under the age of 40. Studies to date have focused primarily on clinical samples, showing that women with dyspareunia report overall sexual impairment, anxiety, and feelings of sexual inadequacy. However, little is known about their body image and genital self-image and few studies have sampled women exclusively from the general population. The aim of the present, controlled study was to investigate body image and genital self-image in a community sample of pre-menopausal women with self-reported dyspareunia. In total, 330 women completed an online survey, of which 192 (58%) had dyspareunia and 138 (42%) were pain-free control women. In comparison to pain-free control women, women with dyspareunia reported significantly more distress about their body image and a more negative genital self-image. Moreover, findings from a logistic regression, in which trait anxiety was controlled for, showed that a more negative genital self-image was strongly and independently associated with an increased likelihood of reporting dyspareunia. These results suggest that, in women with dyspareunia, body image and genital self-image are significantly poorer and would benefit from more attention from both clinicians and researchers.

New approach to managing genital warts.

Lopaschuk CC

Can Fam Physician. 2013 Jul;59(7):731-6.

http://www.ncbi.nlm.nih.gov/pubmed/23851535

OBJECTIVE: To summarize and determine the appropriate use for the new and old management tools for genital warts. SOURCES OF INFORMATION: The following databases were searched: MEDLINE, PubMed, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, ACP Journal Club, and Trip. The bibliographies of retrieved papers were also reviewed. Clinical trials, qualitative review articles, consensus reports, and clinical practice guidelines were retrieved. MAIN MESSAGE: Symptomatic warts are prevalent in at least 1% of the population between the ages of 15 and 49, with estimates of up to 50% of the population being infected with human papillomavirus at some

point in their lifetime. Imiquimod and podophyllotoxin are 2 new treatments for external genital warts that are less painful and can be applied by patients at home. In addition, the quadrivalent human papillomavirus vaccine has been shown to be efficacious in preventing genital warts and cervical cancer. There is still a role for the older treatment methods in certain situations, such as intravaginal, urethral, anal, or recalcitrant warts; or for pregnant patients. CONCLUSION: The new treatments of external genital warts can reduce the pain of treatment and the number of office visits. Other treatment methods are still useful in certain situations.

Therapist-aided exposure for women with lifelong vaginismus: A randomized waiting-list control trial of efficacy.
Ter Kuile MM, Melles R, de Groot HE, Tuijnman-Raasveld CC, van Lankveld JJ
J Consult Clin Psychol. 2013 Sep 23. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24060195

Objective: Vaginismus is commonly described as a persistent difficulty in allowing vaginal entry of a penis or other "objects" (e.g., tampons, fingers, speculum). Lifelong vaginismus is diagnosed when a woman has never been able to have intercourse. The aim of this study was to investigate the efficacy of therapist-aided exposure for lifelong vaginismus. Method: Seventy women and their partners were randomly allocated to exposure or a waiting-list control period of 3 months. The main outcome measure (intercourse ability) was assessed daily during 12 weeks. Secondary outcome measures were complaints about vaginismus, coital pain, coital fear, sexual distress, and sexual functioning. The exposure treatment consisted of a maximum of three 2-hr sessions during 1 week at a university hospital. Each participant performed vaginal penetration exercises herself, in the presence of her partner and a female therapist. Two follow-up sessions were scheduled over a 5-week period. Results: Thirty-one out of 35 (89%; 95% CI [72%, 96%]) participants reported having had sexual intercourse at post-treatment compared with 4 out of 35 (11%; 95% CI [4%, 28%]) participants in the control condition. In most of the successfully treated women (90%), intercourse was possible within the first 2 weeks of treatment. Moreover, treatment resulted in clinical improvement regarding other symptoms related to vaginismus, coital fear, coital pain, and sexual distress. No treatment effects were found regarding other aspects of sexual functioning in women or their partners. Conclusions: This study provides evidence of the efficacy of therapist-aided exposure therapy for women with lifelong vaginismus.

Surgically shortened vagina lengthened by laparoscopic davydov procedure.
Moriarty CR, Miklos JR, Moore RD
Female Pelvic Med Reconstr Surg. 2013 Sep-Oct;19(5):303-5. doi: 10.1097/SPV.0b013e3182a11ae8.
http://www.ncbi.nlm.nih.gov/pubmed/23982582

BACKGROUND: The laparoscopic Davydov procedure is a neovagina surgical technique most commonly used in patients with vaginal agenesis. We present a unique case of vaginal length restoration using this procedure in a patient with vaginal shortening after multiple vaginal surgeries. CASE: A 62-year-old patient presented to our office after multiple vaginal surgeries with symptoms suggestive of cystocele, rectocele, vaginal vault prolapse, and dyspareunia. Excessive vaginal shortening and a painful vaginal apex were also noted upon initial examination. A laparoscopic Davydov procedure was performed to lengthen the vagina and to eliminate the apical pain. CONCLUSION: The laparoscopic Davydov procedure is a surgical option for patients with surgically shortened vaginas and dyspareunia.

Ultra-low-dose vaginal estrogen tablets for the treatment of postmenopausal vaginal atrophy.
Simon JA, Maamari RV
Climacteric. 2013 Aug;16 Suppl 1:37-43. doi: 10.3109/13697137.2013.807606.
http://www.ncbi.nlm.nih.gov/pubmed/23848490

Vaginal atrophy is a common chronic condition affecting up to 57% of postmenopausal women. The decrease in estrogen following cessation of menses can lead to bothersome symptoms that include vaginal dryness and irritation, pain and burning during urination (dysuria), urinary tract infections, and pain (dyspareunia) and bleeding during sexual activities. These symptoms can be safely and effectively managed with the use of local estrogen therapy,

which reduces the risks associated with long-term systemic hormone therapy. The ultra-low-dose 10 µg estradiol vaginal tablet is the lowest approved dose available and has an annual estradiol exposure of only 1.14 mg. Its development addresses recommendations from regulatory agencies and women's health societies regarding the use of the lowest hormonal dose. The 10 µg vaginal tablet displays minimal estradiol absorption, causes no increased risk of endometrial hyperplasia or carcinoma, and provides significant symptom relief. The clinical evidence presented here may offer greater reassurance to health-care professionals and postmenopausal women that vaginal atrophy can be treated safely and effectively.

Tissue-selective estrogen complexes for postmenopausal women.
Mirkin S, Komm BS
Maturitas. 2013 Jul 10. pii: S0378-5122(13)00187-4. doi: 10.1016/j.maturitas.2013.06.003. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23849704

Although hormone therapy using estrogens plus progestogens (EPT) is effective for the management of menopausal symptoms (e.g., vasomotor symptoms and vulvar/vaginal atrophy) and prevention/treatment of postmenopausal osteoporosis, EPT is associated with safety and tolerability concerns. A new alternative to EPT is the tissue selective estrogen complex (TSEC), which partners a selective estrogen receptor modulator (SERM) with one or more estrogens and is designed to treat menopausal symptoms and prevent postmenopausal osteoporosis without the tolerability concerns associated with EPT. The first TSEC to reach advanced clinical development is a combination of the SERM bazedoxifene (BZA) with conjugated estrogens (CE). BZA has been shown to inhibit the stimulatory activity of CE on uterine tissue and breast in vitro and in vivo. In clinical studies, BZA/CE treatment has been associated with significant improvements in menopausal symptoms including hot flushes and vulvar/vaginal atrophy and significant increases in bone mineral density, coupled with reductions in bone turnover marker levels and improvements in sleep and health-related quality of life. Additionally, BZA/CE has been shown to have a neutral effect on endometrial and breast tissue because BZA inhibits the stimulatory effects of estrogens in tissue-selective fashion in these 2 organs. Taken together, results of these preclinical and clinical studies indicate that the benefits of estrogens for treating menopausal symptoms are maintained with BZA/CE without endometrial or breast stimulation, resulting in a safe and effective treatment for symptomatic postmenopausal women.

The CLOSER (CLarifying Vaginal Atrophy's Impact On Sex and Relationships) survey: Implications of vaginal discomfort in postmenopausal women and in male partners.
Nappi RE, Kingsberg S, Maamari R, Simon J
J Sex Med. 2013 Sep;10(9):2232-41. doi: 10.1111/jsm.12235.
http://www.ncbi.nlm.nih.gov/pubmed/23809691

INTRODUCTION: Postmenopausal vaginal atrophy (VA) is a chronic condition with symptoms that include vaginal dryness, soreness, itching, burning, and dyspareunia. AIM: The Clarifying Vaginal Atrophy's Impact On Sex and Relationships survey evaluated the impact of VA on the physical and emotional aspects of sexual relationships between postmenopausal women and their male partners. METHODS: Four thousand one hundred females and 4,100 males representing the United Kingdom, Finland, Norway, Sweden, Denmark, Italy, France, Canada, and the United States were surveyed. Assessments included: (i) talking about VA and its symptoms; (ii) the impact of VA on intimacy, relationships, and women's self-esteem; (iii) talking about VA and erectile dysfunction (ED); and (iv) the impact of local estrogen therapy (LET) on intimacy and relationships. MAIN OUTCOME MEASURES: Descriptive data on the impact of VA. RESULTS: Twenty-eight percent of women did not tell their partners when they first encountered vaginal discomfort, mainly because they felt "it was just a natural part of growing older" (52%) or because of "embarrassment" (21%). Eighty-two percent of males wanted their partner to share their experiences with VA; males were also more comfortable discussing VA than females (68% vs. 58%, respectively). Having sex less often (women: 58%, men: 61%), less satisfying sex (women: 49%, men: 28%), and putting off having sex (women: 35%, men: 14%) were the main effects of VA. Intimacy avoidance was attributed to painful sex (women: 55%, men: 61%) and women's reduced sexual desire (women: 46%, men: 43%). Discussions about vaginal discomfort and ED were generally limited to partners and healthcare providers (HCPs). LET use resulted in less painful sex (women: 62%, men: 59%) and more satisfying sex (women: 47%,

men: 49%). CONCLUSIONS: VA has an adverse emotional and physical impact on postmenopausal women and their partners. These findings may encourage more open communication about VA between couples and their HCPs.

An unusual presentation of a urethral diverticulum as a vaginal wall mass: A case report.
Billow M, James R, Resnick K, Hijaz A
J Med Case Rep. 2013 Jul 1;7(1):171. doi: 10.1186/1752-1947-7-171.
http://www.ncbi.nlm.nih.gov/pubmed/23815779

INTRODUCTION: The diagnosis of urethral diverticulum can be challenging given the vague or absent presenting symptoms. In addition, vaginal cancer can present with elusive symptoms--some parallel to urethral diverticula. A case of a bleeding ulcerated mass anticipated to be a vaginal cancer was instead identified as a benign urethral diverticulum. To the best of our knowledge, this is the first case report of a benign urethral diverticulum presenting as a bleeding, necrotic ulcerated mass. CASE PRESENTATION: A 52 year-old multiparous African-American woman presented with a 2-day history of heavy vaginal bleeding passing large clots and suprapubic pain. A pelvic examination revealed blood clots in the vagina along with a friable, fibrous ulcerated lesion on the anterior suburethral vagina, just left of the midline measuring 4 × 2cm. Initially, this mass was considered to be a vaginal cancer. Intraoperative diagnosis of a benign urethral diverticulum was made. CONCLUSIONS: The diagnosis of urethral diverticula based on the vast array of presenting symptoms, is difficult. This original case report may benefit both gynecologic oncologists and female pelvic surgeons and reconstructive surgeons to keep urethral diverticulum in the differential diagnosis when faced with a bleeding midline anterior vaginal mass. This unusual presentation of a urethral diverticulum demonstrates how similarly it may present to a vaginal cancerous mass.

Herlyn Werner Wunderlich Syndrome: An unusual presentation of acute vaginal pain.
Beer WM, Carstairs SD
J Emerg Med. 2013 Oct;45(4):541-3. doi: 10.1016/j.jemermed.2013.03.035.
http://www.ncbi.nlm.nih.gov/pubmed/23810118

BACKGROUND: Herlyn Werner Wunderlich Syndrome (HWWS) is a congenital abnormality of the Müllerian duct system resulting in uterovaginal duplication, obstructive hemivagina, and ipsilateral renal agenesis. It typically presents shortly after menarche with gradual onset of progressive pelvic pain. CASE REPORT: We report a case of a 19-year-old female who presented to the Emergency Department with sudden onset of severe vaginal pain that was determined to be due to hematocolpos; imaging confirmed the diagnosis of HWWS. CONCLUSIONS: To the best of our knowledge abrupt onset of vaginal pain due to HWWS has not been reported previously. We present this case to increase awareness among emergency physicians of this rare and interesting entity.

Outcomes of a comprehensive nonsurgical approach to pelvic floor rehabilitation for urinary symptoms, defecatory dysfunction, and pelvic pain.
Starr JA, Drobnis EZ, Lenger S, Parrot J, Barrier B, Foster R
Female Pelvic Med Reconstr Surg. 2013 Sep-Oct;19(5):260-5. doi: 10.1097/SPV.0b013e31829cbb9b.
http://www.ncbi.nlm.nih.gov/pubmed/23982573

OBJECTIVE: The authors' intent was to determine the clinical efficacy of comprehensive pelvic floor rehabilitation among women with symptoms of pelvic floor dysfunction (PFD). METHODS: We performed a retrospective analysis of women referred to an academic female pelvic medicine and reconstructive surgery practice for PFD. Data were gathered from the records of 778 women referred for pelvic floor therapy for urinary, bowel, pelvic pain, and sexual symptoms over the course of 4 years. RESULTS: Patients who completed at least 5 therapy sessions reported a mean symptom improvement of 80% in each of the 3 main categories analyzed, namely, urinary incontinence, defecatory dysfunction, and pelvic pain. CONCLUSIONS: Comprehensive, non-operative management of PFD including pelvic floor muscle training, biofeedback, electrogalvanic stimulation, constipation management, behavioral modification, incontinence devices, and pharmacotherapy including vaginal estrogen is effective in the treatment of women with PFD

Tissue selectivity of ospemifene: Pharmacologic profile and clinical implications.
Kangas L, Unkila M
Steroids. 2013 Sep 18. pii: S0039-128X(13)00199-2. doi: 10.1016/j.steroids.2013.09.003. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24055829

The multifactorial consequences of menopausal estrogen deficiency affect numerous tissues throughout the body. Supplemental hormonal therapies carry the burden of a risk/benefit ratio that must be highly individualized. Selective estrogen receptor modulators (SERMs) are estrogen receptor (ER) agonist/antagonists designed to induce benefits comparable with estrogen while minimizing adverse effects. Here, we review the estrogen agonist/antagonist profile of ospemifene, a novel triphenylethylene derivative recently approved to treat dyspareunia, a symptom of vulvar and vaginal atrophy (VVA) due to menopause, both pre-clinically and clinically. Ospemifene binds ERα and ERβ with approximately equal affinities. In preclinical models, ospemifene increased vaginal and uterine epithelial thickness and mucification to the same extent as estrogen. Ospemifene did not induce endometrial hyperplasia in animal models; there also was no stimulatory effect on endometrial cells. In rat and human mammary cells in vitro, ospemifene evokes a dose-dependent inhibition on estrogen-induced cell responses and cell proliferation, supporting an anti-estrogenic effect in breast. In contrast, ospemifene has an estrogenic effect on bone, as seen by improved bone mineral density, strength, mass, and histomorphometry in preclinical models, consistent with improvements in markers of bone resorption and formation in postmenopausal women. Based on the preclinical evidence, ospemifene has beneficial estrogen-like effects on the vaginal epithelium, preliminary evidence to support a neutral endometrial profile, anti-proliferative effects in breast, and estrogenic effects in bone. Taken together, especially regarding estrogen-like effects on the vaginal epithelium, ospemifene presents a profile of tissue-specific effects that appear novel among available SERMs and well-suited for the treatment of VVA.

The outcome of transobturator anterior vaginal wall prolapse repair using porcine dermis graft: Intermediate term follow-up.
Mahdy A, Karp D, Davila GW, Ghoniem GM
Int Braz J Urol. 2013 Jul-Aug;39(4):506-12. doi: 10.1590/S1677-5538.IBJU.2013.04.08.
http://www.ncbi.nlm.nih.gov/pubmed/24054379

Introduction and Hypothesis: We evaluated the anatomical success and complications of Perigee® with porcine dermis Graft in the repair of anterior vaginal wall prolapse (AVWP) Materials and Methods: After Institutional Review Board (IRB) approval, the charts of all patients who underwent AVWP repair using the Perigee/InteXen® kit from July 2005 to July 2009 were reviewed. Patients who had less than 6-month follow-up were excluded. Preoperative data including patient age, previous AVWP repairs, hysterectomy status, preoperative dyspareunia and pertinent physical findings were collected and recorded. Postoperative success was defined as anatomical stage 0 or I using the Pelvic Organ Prolapse Quantification (POP-Q) scoring system. Graft related complications were also recorded. Results: Out of 89 patients, 69 completed at least 6-month follow-up. Median follow-up was 13 (6-48) months. Seventeen patients (25%) had previous AVWP repair and 32 (46%) had previous hysterectomy. Preoperatively, AVWP stage II was found in 9 (13%), stage III in 27 (39%) and stage IV in 33 (48%) patients. Anatomic success was found in 48 (69%) patients, with 23 (33%) having stage 0 and 25 (36%) stage I AVWP. Intraoperative complications included incidental cystotomy in one patient and bladder perforation in one. Postoperative complications included vaginal exposure and dyspareunia in one case, wound dehiscence in one and tenderness over the graft arm with dyspareunia in one. Conclusions: The use of porcine dermis in AVWP repair is safe with minimal graft related complications; however, anatomical success is lower than that reported with the use of synthetic grafts.

Management of symptomatic vulvovaginal atrophy: 2013 Position Statement of the North American Menopause Society.

[No authors listed]

Menopause. 2013 Sep;20(9):888-902. doi: 10.1097/GME.0b013e3182a122c2.
http://www.ncbi.nlm.nih.gov/pubmed/23985562

OBJECTIVE: To update and expand the previous position statement of The North American Menopause Society (NAMS) on the management of symptomatic vulvovaginal atrophy (VVA) in postmenopausal women. METHODS: NAMS searched PubMed for medical literature on VVA published since their 2007 position statement on the role of local vaginal estrogen for treatment of vaginal atrophy in postmenopausal women. A panel of acknowledged experts in the field of genitourinary health reviewed the literature to evaluate new evidence on local estrogen as well as on other management options available or in development for symptomatic VVA. The panel's conclusions and recommendations were reviewed and approved by the NAMS Board of Trustees. RESULTS: Symptomatic VVA can significantly impair the quality of life (QOL) of postmenopausal women and may be underdiagnosed. In most cases, it can be managed successfully. A number of over-the-counter and government-approved prescription therapies available in the United States and Canada demonstrate effectiveness, depending on the severity of VVA symptoms. These include vaginal lubricants and moisturizers, vaginal estrogen, hormone therapy, and the selective estrogen-receptor modulator ospemifene (indicated for dyspareunia). Long-term studies on the endometrial safety of local estrogen and ospemifene are lacking. Changes in the vaginal microbiome have various effects on symptoms. CONCLUSIONS: Clinicians can improve the sexual health and QOL of postmenopausal women by educating women about, diagnosing, and appropriately managing symptomatic VVA. Choice of therapy depends on the severity of symptoms, the effectiveness and safety of therapy for the individual patient, and patient preference. Estrogen therapy is the most effective treatment for moderate to severe symptoms, although a direct comparison of estrogen and ospemifene is not available. Non-hormonal therapies available without a prescription provide sufficient relief for most women with mild symptoms. When low-dose estrogen is administered locally, a progestogen is not indicated for women without a uterus and generally is not indicated for women with an intact uterus. However, endometrial safety has not been studied in clinical trials beyond 1 year. There are insufficient data to confirm the safety of local estrogen in women with breast cancer; management of VVA should take the woman's needs and the recommendation of her oncologist into consideration. Research on the vaginal microbiome may lead to other therapies in the future.

Impact of vulvovaginal health on postmenopausal women: A review of surveys on symptoms of vulvovaginal atrophy.

Parish SJ, Nappi RE, Krychman ML, Kellogg-Spadt S, Simon JA, Goldstein JA, Kingsberg SA

Int J Womens Health. 2013 Jul 29;5:437-47. doi: 10.2147/IJWH.S44579.
http://www.ncbi.nlm.nih.gov/pubmed/23935388

Several recent, large-scale studies have provided valuable insights into patient perspectives on postmenopausal vulvovaginal health. Symptoms of vulvovaginal atrophy, which include dryness, irritation, itching, dysuria, and dyspareunia, can adversely affect interpersonal relationships, quality of life, and sexual function. While approximately half of postmenopausal women report these symptoms, far fewer seek treatment, often because they are uninformed about hypo-estrogenic postmenopausal vulvovaginal changes and the availability of safe, effective, and well-tolerated treatments, particularly local vaginal estrogen therapy. Because women hesitate to seek help for symptoms, a proactive approach to conversations about vulvovaginal discomfort would improve diagnosis and treatment.

Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy.

Goldstein SR, Bachmann GA, Koninckx PR, Lin VH, Portman DJ, Ylikorkala O; the Ospemifene Study Group

Climacteric. 2013 Aug 28. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23984673

Abstract Objective-Assessment of 12-month safety of ospemifene 60mg/day for treatment of postmenopausal women with vulvar and vaginal atrophy(VVA). Methods-In this 52-week, randomized, double-blind, placebo-controlled, parallel-group study, women 40-80years with VVA and an intact uterus were randomized 6:1 to ospemifene 60mg/day or

placebo. Primary objective was 12-month safety, particularly endometrial; 12-week efficacy was assessed. Safety assessments included endometrial histology and thickness, and breast and gynecological examinations. Efficacy evaluations included changes from Baseline to Week-12 in percentage of superficial and parabasal cells and vaginal pH. Results-Of 426 randomized subjects, 81.9% (n=349) completed the study with adverse events (AEs) the most common reason for discontinuation (ospemifene-9.5%; placebo-3.9%). Most (88%) treatment-emergent AEs with ospemifene were considered mild or moderate. Three cases (1.0%) of active proliferation were observed in the ospemifene group. For one, active proliferation was seen at end of study Week-52, and diagnosed as simple hyperplasia without atypia on follow-up biopsy 3 months after last dose. This subsequently resolved with progestogen treatment and dilatation and curettage. In six subjects (5 ospemifene [1.4%], 1 placebo [1.6%]) endometrial polyps were found (histopathology); however, only one (ospemifene) was confirmed as a true polyp during additional expert review. Endometrial histology showed no evidence of carcinoma. Statistically significant improvements were seen for all primary and secondary efficacy measures and were sustained through Week-52 with ospemifene vs. placebo. Conclusions-Findings of this 52-week study confirm tolerance and efficacy of oral ospemifene previously reported in short- and long-term studies.

The association of dysmenorrhea with noncyclic pelvic pain accounting for psychological factors.
Westling AM, Tu F, Griffith JW, Hellman KM
Am J Obstet Gynecol. 2013 Aug 22. pii: S0002-9378(13)00860-0. doi: 10.1016/j.ajog.2013.08.020. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23973396

OBJECTIVE: The factors that underlie pelvic pain are poorly understood. Specifically, the relative influence of dysmenorrhea and psychological factors in the etiology of noncyclic pelvic pain conditions, such as interstitial cystitis and irritable bowel syndrome, is unknown. To further characterize pelvic pain, we compared the frequency of menstrual, somatosensory, and psychological risk factors between women with and without severe noncyclic pelvic pain symptoms. STUDY DESIGN: A total of 1012 reproductive-aged women completed a 112-item questionnaire with domains including mood, fatigue, physical activity, somatic complaint, and pain. Questionnaire items included existing items for menstrual distress and newly written items derived from qualitative interviews. The relationship of dysmenorrhea and noncyclic pelvic pain complaints (dyspareunia, dyschezia, or dysuria) was modeled using quantile regression. RESULTS: Among women who menstruate regularly, those with dysmenorrhea had disproportionally more severe noncyclic pelvic pain (54/402, 13%) than women without dysmenorrhea (5/432, 1%; odds ratio, 13; 95% confidence interval, 5-33). In a multivariate-adjusted model, dysmenorrhea (β = .17), activity capability (β = .17), somatic complaint (β = .17), and bodily pain (β = .12) were the primary predictors of noncyclic pelvic pain. Depression (β = .03) and anxiety (β = .01) were not significantly predictive. The presence of dysmenorrhea, somatic complaint, and low activity capability predicted 90% of the cases of women with noncyclic pelvic pain. CONCLUSION: The association between dysmenorrhea and noncyclic pelvic pain suggests that menstrual pain is an etiological factor in noncyclic pelvic pain, whereas depression and anxiety may be secondary effects. Longitudinal studies are needed to determine whether dysmenorrhea causally influences development of noncyclic pelvic pain or shares common underlying neural mechanisms.

Colostrum in menopause effects on vaginal cytology/symptoms.
Tucci S, Mancini R, De Vitis C, Noto A, Marra E, Lukic A, Giovagnoli MR, Moscarini M
Clin Exp Obstet Gynecol. 2013;40(2):219-21.
http://www.ncbi.nlm.nih.gov/pubmed/23971242

The aim of this study was to assess the effects of three weeks of daily colostrum cream on vaginal cytology and local symptoms related to menopause. Genito-urinary symptoms and cell morphology were analyzed at time 0 (T0) and after three weeks (16 +/- days since the end of treatment) at time 1 (T1). Dyspareunia, vaginal dryness, and maturation index (MI) reached a statistically significant difference between T0 and T1. The results proved to be an alternative treatment for vaginal distress caused by lack of hormones in patients in which hormonal treatment is contraindicated.

Sexual functions of Turkish women with gynecologic cancer during the chemotherapy process.
Akkuzu G, Ayhan A
Asian Pac J Cancer Prev. 2013;14(6):3561-4.
http://www.ncbi.nlm.nih.gov/pubmed/23886145

BACKGROUND:The negative effects of gynecologic cancer on women's health is multidimensional. Sexual problems arising after chemotherapy are decreased interest and vaginal lubrication, lack of orgasm and dyspareunia and sense of reduction in sexual attractiveness in general. The purpose of this study was to evaluate changes that patients who receive chemotherapy for a gynecologic oncology disorder experience in their sexual functions. MATERIALS AND METHODS: A descriptive/cross-sectional and qualitative study was performed. The Female Sexual Function Index (FSFI) was used in order to collect data on sexual capacity. The quantitative data obtained were evaluated with frequency and percentage calculations while content analysis was performed for the qualitative data. RESULTS: All of the information related to sexuality was provided by the physician. Chemotherapy treatment affected sexuality negatively in 55.9%. Since receiving the diagnosis, 52.9% of women had experienced no sexual intercourse at all. Those who had an FSFI score of 30 and below made up 75% of the women. After the content analysis of data obtained during in in-depth interviewing, we focused on three main themes: desire for sexual intercourse, problems experienced during sexual intercourse, and coping with problems. CONCLUSIONS: An integrated system where sexual problems can be handled professionally should be present during gynecological cancer treatment.

Sex therapy for female sexual dysfunction.
Pereira VM, Arias-Carrión O, Machado S, Nardi AE, Silva AC
Int Arch Med. 2013 Sep 26;6(1):37. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24066697

INTRODUCTION: About 45% of women suffer from some form of sexual dysfunction. Despite its high prevalence, there are few studies that have systematically evaluated sex therapy in comparison with other interventions. OBJECTIVE: Review randomized clinical trials that present psychotherapeutic interventions for female sexual dysfunctions. METHOD: Through a search in three databases (Medline, Web of Science and PsycInfo), 1419 references were found. After an analysis of the abstracts, twenty-seven articles met the inclusion criteria and composed this review. RESULTS: Sex therapy, as proposed by Masters and Johnson and Heiman and LoPiccolo, is still the most commonly used form of therapy for sexual dysfunctions; although it has shown results, the results do not consistently support that this is the best alternative in the treatment of sexual dysfunctions. CONCLUSION: There is a lack of systematic study of many female sexual dysfunctions. Orgasmic disorder and sexual pain (vaginismus and dyspaurenia) are the most extensively studied disorders and those in which sex therapy seems to have better outcomes.

Arriving at the diagnosis of female sexual dysfunction.
Latif EZ, Diamond MP
Fertil Steril. 2013 Sep 4. pii: S0015-0282(13)02951-8. doi: 10.1016/j.fertnstert.2013.08.006. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24012196

Female sexual dysfunctions include a group of sexual complaints and disorders affecting women of all ages, and stemming from a heterogeneous array of etiologies and contributing factors. The classification system for sexual dysfunctions in the woman has evolved from a linear categorization of sexual desire, arousal, orgasm, and pain disorders to one that is more complex and overlapping. Personal distress is a key factor in defining a sexual problem as a dysfunction. The recently released Diagnostic and Statistical Manual of Mental Disorders, edition 5, collapses former definitions of female sexual disorders and moves away from the older linear model of diagnostic categories. Physicians should be open to discussing sexual problems with women, and may make use of validated questionnaires in the office setting. Evaluation tools available for assessing sexual function in the woman are in use in the research setting, as are physiological measures of assessment.

Efficacy of ravuconazole in a murine model of vaginitis by Candida Albicans.
Elizondo-Zertuche M, Robledo-Leal E, González JG, Ceceñas LA, González GM
Rev Iberoam Micol. 2013 Sep 23. pii: S1130-1406(13)00085-5. doi: 10.1016/j.riam.2013.09.006. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24071640

BACKGROUND: The incidence of vulvovaginal candidiasis, a common infection among healthy women primarily caused by the yeast Candida albicans, has increased significantly in recent years. AIMS: The purpose of this study was to compare the efficacy of ravuconazole (RVC) and fluconazole (FLC) in the treatment of experimental C. albicans vaginitis. METHODS: Forty isolates of C. albicans were screened for their in vitro susceptibility to RVC and FLC. A strain of C. albicans that was resistant to FLC (minimum inhibitory concentration [MIC] of >64μg/ml) was selected for the in vivo study. Treatment regimens for the murine vaginal infection model were 1) 1, 5, 10, and 20mg/kg RVC once daily, 2) 20mg/kg RVC twice daily, 3) 20mg/kg FLC once daily, and 4) 20mg/kg FLC twice daily. RESULTS: The geometric means of the MIC values at 48h for all isolates tested were 0.05 and 0.5μg/ml for RVC and FLC, respectively. Regimens of either RVC or FLC at 20mg/kg twice daily were more effective at reducing the load of FLC-resistant C. albicans than single dose administration. CONCLUSIONS: Sterilization of the vagina was not observed with RVC or FLC treatment in the animal model, although RVC treatment showed a lower fungal concentration 14 days after drug administration.

NDV-3 protects mice from vulvovaginal candidiasis through T- and B-cell immune response.
Ibrahim AS, Luo G, Gebremariam T, Lee H, Schmidt CS, Hennessey JP Jr, French SW, Yeaman MR, Filler SG, Edwards JE Jr
Vaccine. 2013 Sep 21. pii: S0264-410X(13)01247-4. doi: 10.1016/j.vaccine.2013.09.016. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24063977

We have previously reported that vaccination with rAls3p-N protein of Candida albicans, formulated with alum adjuvant (also designated as NDV-3) protects immune-competent mice from, lethal disseminated candidiasis and mucosal oropharyngeal candidiasis. NDV-3 vaccine was recently, tested in a Phase 1 clinical trial and found to be safe, well-tolerated, and induced robust humoral and, cellular immune responses with increased interferon (IFN)-gamma and interleukin (IL)-17 secretion. In preparation for a Phase 2 clinical trial against vulvovaginal candidiasis (VVC), we evaluated NDV-3, efficacy in a murine VVC model. Here, NDV-3 induced a strong immune response characterized by high, anti-rAls3p-N serum IgG and vaginal IgA titers. Furthermore, moderate doses of the vaccine (a range of 1-30μg given subcutaneously [SQ] or 0.3-10μg given intramuscularly [IM]) elicited a 10-1000 fold, decrease in vaginal fungal burden vs. control (mice injected with alum adjuvant alone) in both inbred, and outbred mice infected with different clinical C. albicans isolates. Additionally, NDV-3 required both, T and B lymphocytes for efficacy in reducing C. albicans tissue burden, which is followed by a reduction, in neutrophil influx to the affected site. Finally, anti-rAls3p-N antibodies enhanced the ex vivo killing, of C. albicans by neutrophils primed with IFN-gamma. These data indicate that NDV-3 protects mice, from VVC by a mechanism that involves the concerted priming of both humoral and adaptive immune, responses.

Genital pyoderma gangrenosum: Report of two cases and published work review of Japanese cases.
Satoh M, Yamamoto T
J Dermatol. 2013 Oct;40(10):840-843. doi: 10.1111/1346-8138.12252. Epub 2013 Aug 21.
http://www.ncbi.nlm.nih.gov/pubmed/24033392

Pyoderma gangrenosum is an ulcerative skin disorder showing characteristic non-infectious ulcers and affects the lower extremities in approximately 70% of cases. Pyoderma gangrenosum is commonly associated with systemic diseases such as inflammatory bowel disease, rheumatoid arthritis and hematological malignancies. Herein, we report two cases of Japanese patients diagnosed with genital pyoderma gangrenosum. Case 1 was a 74-year-old woman without associated systemic complications, whose skin lesion resembled a squamous cell carcinoma and was limited to the vulva. Case 2 is an 89-year-old man, who suffered from myelodysplastic syndrome and acute myeloid leukemia, and presented with penile and leg ulcers mimicking pressure sores. Both cases responded well to systemic steroids. We review 13 genital pyoderma gangrenosum cases (76.9% male; aged 30-89 years) from 1996 to 2012 in Japan, including 11 previously reported cases and the present study's two cases. Four of the 13 genital pyoderma gangrenosum cases had associated

systemic diseases and their skin lesions spread to the extra-genital areas. Eight of the remaining nine genitalia-localized pyoderma gangrenosum cases had no associated systemic diseases. In conclusion, genital pyoderma gangrenosum is rare and may be misdiagnosed. It should therefore be considered in cases of refractory genital ulcers. In addition, genitalia-localized pyoderma gangrenosum tends to be without systemic complications.

Low-concentration topical tacrolimus for the treatment of anogenital lichen sclerosus in childhood: Maintenance treatment to reduce recurrence.
Li Y, Xiao Y, Wang H, Li H, Luo X
J Pediatr Adolesc Gynecol. 2013 Aug;26(4):239-42.
http://www.ncbi.nlm.nih.gov/pubmed/24049806

BACKGROUND: Lichen sclerosus (LS) is a chronic inflammatory skin disorder that is commonly found in the anogenital area, especially in females. Ultra-potent topical corticosteroids are first line for the treatment of LS, but their atrophic side effects and the recurrence of the disease restrict their use. An equally effective, safer, tolerant therapeutic option is required, especially in the treatment and preventing relapse of children. METHODS: Fourteen pre-pubertal girls (range of age: 4 to 11 years) with anogenital lichen sclerosus were treated with 0.03% tacrolimus ointment twice daily for 16 weeks, then 9 of the 14 patients adhered to 2 times weekly for further 6 months (a total of 10 months). The therapeutic effects were evaluated according to 3 grades: complete response (O75% improvement, partial response (30%-75% improvement),or no response (!30% improvement). RESULTS: Clinical improvement occurred in all patients (100%). Complete response of symptoms and signs was achieved in 5 (36%), 9 (64%) and 11 (79%) patients at week 8, week 16, and month 10 respectively. During the follow-up period of 1 year, 4 patients (4/5, 80%) who treated with tacrolimus ointment for 16 weeks had a recurrence of symptoms, while only 2 of 9 (22%) patients who insisted on maintenance therapy developed recurrence of disease. No severe side effects were observed. CONCLUSIONS: Low-concentration topical tacrolimus appears to be an effective and safe treatment for children with anogenital lichen sclerosus. Maintenance therapy (2 times a week for 6 months) can reduce the relapse of the disease.

Differential gene hypermethylation in genital lichen sclerosus and cancer: A comparative study.
Guerrero-Setas D, Pérez-Janices N, Ojer A, Blanco-Fernandez L, Guarch-Troyas C, Guarch R
Histopathology. 2013 Jun 17. doi: 10.1111/his.12204. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23998425

AIMS: Lichen sclerosus (LS) is a chronic inflammatory disease of the genital skin of unknown aetiology. The role of LS in penile squamous cell carcinogenesis is not well characterized. HPV has been implicated in both, as have epigenetic changes. The presence of HPV and hypermethylation of the MGMT, p16, RASSF1, RASSF2, TSLC1 and TSP1 genes were studied in penile LS; MGMT, RASSF2 and TSLC1 hypermethylation in penile cancer and TSLC1 hypermethylation in vulvar LS and cancer extends previous results reported by our group. METHODS AND RESULTS: Thirty-seven HPV genotypes and hypermethylation were evaluated by PCR/reverse-line-blot and methylation-specific PCR respectively, in 27 preputial LS, 24 penile SCC, 30 vulvar SCC, 21 vulvar LS and 22 normal skin cases. HPV66 was present in 3.7% of penile LS cases, and p16 and RASSF2 hypermethylation were more frequent in penile cancer than in penile LS. p16, RASSF1, RASSF2 and TSP1 hypermethylation were similar in penile and vulvar LS. CONCLUSIONS:` Gene hypermethylation is a common event in penile LS, and occurs approximately as frequently as in vulvar LS. Certain genes can be hypermethylated as an early or late event in LS or cancer, respectively. This suggests a possible sequential role for these alterations in the transition from benign to malignant lesions.

Vulvo-vaginitis in prepubertal girls: New ways of administering old drugs.
Tartaglia E, Giugliano B, Ucciferri C, Giannattasio A, Giuliano P, Iannaccone VL, Pisani F, Mastrantonio P
J Pediatr Adolesc Gynecol. 2013 Oct;26(5):277-80. doi: 10.1016/j.jpag.2013.05.003.
http://www.ncbi.nlm.nih.gov/pubmed/24012128

STUDY OBJECTIVE: To evaluate the effectiveness and safety of local vs systemic antibiotic treatment in the management of recurrent vulvovaginitis in children. DESIGN: Randomized treatment and follow-up of 90 cases of persistent vulvovaginitis. SETTING: The Department of Medicine and Health Sciences, Institute of Gynecology and Obstetrics, University of Molise, Italy. METHODS: Between January 2009 and December 2012, 90 prepubertal girls (Tanner Stage I) aged 6-12 years, with recurrent discharge not responding to common hygienic measures and not suspected of being sexually abused, were treated, 45 patients with oral antibiotic treatment (group 1) and 45 patients with a local antibiotic treatment (group 2). Vaginal cultures were prepared before treatment and follow-ups were made after 3 months. RESULTS: Bacterial pathogens were isolated in vaginal secretions of 84/90 (93%) girls. There were 6 girls receiving antibiotic treatment who had persistent discharge and repetitive isolations of Escherichia coli. Administration type was selected at random. Symptoms and signs were resolved in all girls, but we observed 1 recurrence (2.22%) in group 2 vs 6 recurrences (13.33%) in group 1 (P = .049). In group 1 we observed 3 cases (6.67%) of gastro-intestinal side effects vs no cases in group 2 (P = .079). CONCLUSION: Topical medication based on netilmicin, associated with Benzalkonium-Chloride, showed a clinical and microbiological effectiveness in first-line treatment of bacterial vulvovaginitis in children, comparable to conventional drugs; so local treatment may be a good alternative to systemic treatment decreasing the use of oral antibiotics in young people and related risks of bacterial resistances.

Lichen sclerosus associated with perineal urethrostomy.
Shim TN, Andrich DE, Mundy AR, Bunker CB
Br J Dermatol. 2013 Sep 6. doi: 10.1111/bjd.12617. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24032997

We welcome the paper by Al-Niaimi and Lyon[1] describing peri urostomal lichen sclerosus (LSc). Their findings further bolster the theory that has been promulgated by CBB for the last decade that genital LSc is due to occluded exposure of susceptible epithelium to urine.

Emergence of non-Albicans Candida among candidal vulvovaginitis cases and study of their potential virulence factors, from a tertiary care center, north India.
Kumari V, Banerjee T, Kumar P, Pandey S, Tilak R
Indian J Pathol Microbiol. 2013 Apr-Jun;56(2):144-7. doi: 10.4103/0377-4929.118703.
http://www.ncbi.nlm.nih.gov/pubmed/24056652

Purpose: The purpose of this study was to determine the prevalence of various Candida species and study some of their virulence factors among the vulvovaginal candidiasis (VVC) patients. Study Design and Settings: The study was conducted in a Tertiary Care University Hospital in North India. Materials and Methods: This study was carried out prospectively for a period of 1 year. High vaginal swabs (HVSs) were collected from women in childbearing age group attending the gynecology and obstetrics out-patient departments with the complaints suggestive of vulvovaginitis. Samples were plated on Sabouraud's dextrose agar slope. Candida spp. isolated was further speciated based on microscopy, biochemical tests and culture characteristics on special media. Virulence factors of these strains were determined by biofilm formation and phospholipase activity. Result: A total of 464 HVS from 232 patients with the complaints of vulvovaginitis were included in this study. Following laboratory workup, 71 specimens were positive for genus Candida (30.6%). Further speciation showed 32.4% as Candida albicans, 45.07% Candida parapsilosis and 22.53% of Candida glabrata. Biofilm production was shown by 50 candidal strains (70.4%) and phospholipase activity was given by 41 candidal strains (57.74%). Conclusion: Our study suggests increasing prevalence of non-albicans Candida among the VVC cases along with their virulence factors. Therefore, we recommend that microbiological investigation upto species level should be mandatory to determine the emergence of non-albicans Candida as a major cause of VVC.

Evaluation of mucoadhesive gels with propolis (EPP-AF) in preclinical treatment of candidiasis vulvovaginal infection.
Berretta AA, de Castro PA, Cavalheiro AH, Fortes VS, Bom VP, Nascimento AP, Marquele-Oliveira F, Pedrazzi V, Ramalho LN, Goldman GH.
Evid Based Complement Alternat Med. 2013;2013:641480. doi: 10.1155/2013/641480. Epub 2013 Aug 7.
http://www.ncbi.nlm.nih.gov/pubmed/23997797

Vulvovaginal candidiasis is the second cause of vaginal infection in the USA. Clinical treatment of C. albicans infections is routinely performed with polyenes and azole derivatives. However, these drugs are responsible for undesirable side effects and toxicity. In addition, C. albicans azole and echinocandin resistance has been described. Propolis is a bee product traditionally used due to its antimicrobial, anti-inflammatory, and other properties. Therefore, the present work aimed to evaluate different propolis presentations in order to evaluate their in vitro and in vivo efficacy. The methodologies involved antifungal evaluation, chemical analysis, and the effects of the rheological and mucoadhesive properties of propolis based gels. The obtained results demonstrated the fungicide action of propolis extracts against all three morphotypes (yeast, pseudohyphae, and hyphae) studied. The highest level of fungal cytotoxicity was reached at 6-8 hours of propolis cell incubation. Among the based gel formulations developed, the rheological and mucoadhesive results suggest that propolis based carbopol (CP1%) and chitosan gels were the most pseudoplastic ones. CP1% was the most mucoadhesive preparation, and all of them presented low thixotropy. Results of in vivo efficacy demonstrated that propolis based gels present antifungal action similar to clotrimazole cream, suggesting that future clinical studies should be performed.

Comparison of nucleic-acid amplification assays with BD Affirm VPIII for the diagnosis of vaginitis/vaginosis in symptomatic women.
Cartwright CP, Lembke BD, Ramachandran K, Body BA, Nye MB, Rivers CA, Schwebke JR
J Clin Microbiol. 2013 Aug 28. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23985917

A commercially available, non-amplified, nucleic-acid probe-based test system (BD Affirm™ VP III) was compared with nucleic-acid amplification (NAA) based assays for determining the etiology of vaginitis in a cohort of 323 symptomatic women. Firstly, a semi-quantitative, multiplexed, PCR assay (BV-PCR) and the Affirm VP III G. vaginalis test were compared with a unified bacterial vaginosis (BV) reference standard incorporating both Nugent Gram-stain scores and Amsel clinical criteria. In the evaluable population of 305 patients, BV-PCR was 96.9% (191/197) sensitive and 92.6% specific (100/108) for BV, whilst Affirm VP III was 90.1% sensitive (179/197) and 67.6% specific (73/108). Secondly, a multiplexed, PCR assay detecting C. albicans and C. glabrata (CAN-PCR) was compared with the Affirm VP III Candida spp. test using a reference standard for vulvovaginal candidiasis (VVC) of yeast culture plus exclusion of alternate vaginitis etiologies. In the population evaluated (n=102), CAN-PCR was 97.7% sensitive (42/43) and 93.2% specific (55/59), and Affirm VP III 58.1% sensitive (25/43) and 100% specific (59/59) for VVC. Finally, the results of a commercial NAA test (GenProbe Aptima® Trichomonas vaginalis assay; ATV) for T. vaginalis were compared with the Affirm VP III T. vaginalis test. In the absence of an independent reference standard for trichomonal vaginitis (TV), a positive result in either assay was deemed to represent true infection. In the evaluable cohort of 388 patients, the sensitivity of ATV was 98.1% (53/54) versus 46.3% (25/54) for Affirm VP III. The diagnostic accuracy of the combined NAA-based test construct was approximately 20-25% higher than the Affirm VPIII when modeled in populations with varying prevalence of infectious vaginitis.

Clotrimazole dampens vaginal inflammation and neutrophil infiltration in response to Candida Albicans infection.
Wilson D, Hebecker B, Moyes DL, Miramón P, Jablonowski N, Wisgott S, Allert S, Naglik JR, Hube B
Antimicrob Agents Chemother. 2013 Oct;57(10):5178-80. doi: 10.1128/AAC.01244-13.
http://www.ncbi.nlm.nih.gov/pubmed/23896471

The pathology of vulvovaginal candidiasis (VVC) caused by Candida albicans is associated with a non-protective inflammatory response and is frequently treated with clotrimazole. We investigated the mechanisms by which clotrimazole resolves VVC. Low levels of clotrimazole, which do not block fungal growth, inhibit expression of a "danger response" transcription factor, c-Fos, block production of pro-inflammatory cytokines, and inhibit neutrophil infiltration to the site of infection.

Identification of the cell targets important for propolis-induced cell death in Candida Albicans.
de Castro PA, Bom VL, Brown NA, Almeida RS, Ramalho LN, Savoldi M, Goldman MH, Berretta AA, Goldman GH
Fungal Genet Biol. 2013 Jul 13. pii: S1087-1845(13)00122-9. doi: 10.1016/j.fgb.2013.07.001. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23856128

Candida albicans is the most common fungal pathogen of humans, forming both commensal and opportunistic pathogenic interactions, causing a variety of skin and soft tissue infections in healthy people. In immunocompromised patients C. albicans can result in invasive, systemic infections that are associated with a high incidence of mortality. Propolis is a complex mixture of several resinous substances which are collected from plants by bees. Here, we demonstrated the fungicidal activity of propolis against all three morphogenetic types of C. albicans and that propolis-induced cell death was mediated via metacaspase and Ras signaling. To identify genes that were involved in propolis tolerance, we screened ~800 C. albicans homozygous deletion mutants for decreased tolerance to propolis. Fifty-one mutant strains were identified as being hypersensitive to propolis including seventeen genes involved in cell adhesion, biofilm formation, filamentous growth, phenotypic switching and pathogenesis (HST7, GIN4, VPS34, HOG1, ISW2, SUV3, MDS3, HDA2, KAR3, YHB1, NUP85, CDC10, MNN9, ACE2, FKH2, and SNF5). We validated these results by showing that propolis inhibited the transition from yeast-like to hyphal growth. Propolis was shown to contain compounds that conferred fluorescent properties to C. albicans cells. Moreover, we have shown that a topical pharmaceutical preparation, based upon propolis, was able to control C. albicans infections in a mouse model for vulvovaginal candidiasis. Our results strongly indicate that propolis could be used as a strategy for controlling candidiasis.

Evaluation of syngonanthus nitens (Bong.) ruhl. Extract as antifungal and in treatment of vulvovaginal candidiasis.
de Freitas Araújo MG, Pacífico M, Vilegas W, Dos Santos LC, Icely PA, Miró MS, Scarpa MV, Bauab TM, Sotomayor CE
Med Mycol. 2013 Oct;51(7):673-82. doi: 10.3109/13693786.2013.795294.
http://www.ncbi.nlm.nih.gov/pubmed/23758104

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

Associations with asymptomatic colonization with candida in women reporting past vaginal candidiasis: An observational study.

Watson CJ, Fairley CK, Grando D, Garland SM, Myers SP, Pirotta M

Eur J Obstet Gynecol Reprod Biol. 2013 Jul;169(2):376-9. doi: 10.1016/j.ejogrb.2013.03.030.
http://www.ncbi.nlm.nih.gov/pubmed/23639675

OBJECTIVE: Asymptomatic vaginal colonization with Candida species is a known risk factor for vulvovaginal candidiasis (VVC). Taking known risk factors for symptomatic VVC, the authors sought to identify factors associated with asymptomatic colonization. DESIGN: As part of a randomized controlled trial which compared vaginal candidal colony counts in women taking garlic tablets or placebo, 192 asymptomatic women collected a baseline screening swab for Candida species. Eligibility for this study included at least one self-reported episode of VVC in the previous 12 months and age 18-50 years. Known risk factors for VVC were compared in women colonized with candida and those without colonization. RESULTS: 37% of asymptomatic women who self-reported VVC in the previous 12 months were colonized with vaginal Candida species. Using multivariate analysis, two factors were associated with asymptomatic colonization: a current sexual partner (P=0.02) and being born outside of Australia (P=0.05). Use of oral contraceptives was not statistically significant (P=0.27). CONCLUSIONS: Clinical relevance of asymptomatic colonization with vaginal yeast and its link to episodes of VVC warrants further investigation.

Prevalence of recurrent vulvovaginal candidiasis in 5 European countries and the United States: Results from an internet panel survey.

Foxman B, Muraglia R, Dietz JP, Sobel JD, Wagner J

J Low Genit Tract Dis. 2013 Jul;17(3):340-5. doi: 10.1097/LGT.0b013e318273e8cf.
http://www.ncbi.nlm.nih.gov/pubmed/23486072

OBJECTIVE: This study aimed to estimate prevalence of vulvovaginal candidiasis (VVC) and recurring VVC (RVVC). MATERIALS AND METHODS: An online omnibus survey was administered to 6,010 women aged 16 and older in 6 countries. RESULTS: We analyzed surveys from 6,000 women. Depending on the country, between 29% and 49% of participating women reported having a health care provider-diagnosed vaginal yeast infection during their lifetime. More than one fifth of women reporting one vaginal yeast infection also reported a 12-month period with 4 or more infections (RVVC) (overall 9%). The cumulative probability of RVVC after an initial vaginal yeast infection was very high. By age 25 years, the probability was 10% for women having had 1 initial yeast infection. By age 50 years, it was 25%. CONCLUSIONS: The overall rates of VVC and RVVC were high and consistent with previous findings. Results were consistent across countries with the exception of France, which had a lower rate of VVC. This may reflect differences in risk behavior, response to infection, or sampling biases. Recurring VVC is a significant health problem in western countries, and the probability that VVC will progress to RVVC is high.

Screening for sexual dysfunction in women diagnosed with breast cancer: Systematic review and recommendations.

Bartula I, Sherman KA

Breast Cancer Res Treat. 2013 Sep;141(2):173-85. doi: 10.1007/s10549-013-2685-9.
http://www.ncbi.nlm.nih.gov/pubmed/24013707

Breast cancer patients are at increased risk of sexual dysfunction. Despite this, both patients and practitioners are reluctant to initiate a conversation about sexuality. A sexual dysfunction screening tool would be helpful in clinical practice and research, however, no scale has yet been identified as a "gold standard" for this purpose. The present review aimed at evaluating the scales used in breast cancer research in respect to their psychometric properties and the extent to which they measure the DSM-5/ICD-10 aspects of sexual dysfunction. A comprehensive search of the literature was conducted for the period 1992-2013, yielding 129 studies using 30 different scales measuring sexual functioning, that were evaluated in the present review. Three scales (Arizona Sexual Experience Scale, Female Sexual Functioning Index, and Sexual Problems Scale) were identified as most closely meeting criteria for acceptable psychometric properties and incorporation of the DSM-5/ICD-10 areas of sexual dysfunction. Clinical implications for implementation of these measures are discussed as well as directions for further research.

Androgen therapy in women: For whom and when.
Pluchino N, Carmignani A, Cubeddu A, Santoro A, Cela V, Alcalà TE
Arch Gynecol Obstet. 2013 Oct;288(4):731-7. doi: 10.1007/s00404-013-2969-7.
http://www.ncbi.nlm.nih.gov/pubmed/23912530

Androgens play a primary role in female physiopathology. The age-related reduction in the production of ovarian and adrenal androgens may significantly affect women's health. The decline of circulating androgens results from a combination of two events: reduced ovarian production and aged-related decline in adrenal androgen synthesis. The relative androgen deficiency in pre- and postmenopausal women may induce impairment of sexual function, libido, well-being, energy and may contribute to reduced cognitive functions. Whether androgen deficiency also affects cardiovascular or bone biology in women during reproductive aging is still controversial. Both in the central nervous system and peripheral tissues, there are multiple ways whereby androgens target their specific actions through a particular tropism of the brain areas that are involved in sexual function, behavior and cognition. Among circulating available androgens that are involved in several domains of sexual response, adrenal androgens seem to be related to some sexual symptoms as well as diminished cognitive function in postmenopausal women. The possibilities of treating low sexual desire/hypoactive sexual desire disorder are multifaceted and should include the combination of both pharmacological treatments able to maximize biological signals that drive the sexual response as well as individualized psychosocial therapies to overcome personal and relational difficulties. Transdermal testosterone has been proved to be effective but the use of additional treatment like oral or vaginal dehydroepiandrosterone is still controversial, despite many evidences support it. The decision to treat premenopausal or postmenopausal women with signs/symptoms of androgen insufficiency is mainly based on the clinical judgment, together with estrogens co-administration and following informed consent related to the unknown long-term risks.

Sexual dysfunction in women with cancer.
Falk SJ, Dizon DS
Fertil Steril. 2013 Oct;100(4):916-21. doi: 10.1016/j.fertnstert.2013.08.018.
http://www.ncbi.nlm.nih.gov/pubmed/24011609

Approximately 14 million people have a history of cancer in the United States alone, and the number is expected to increase with time. This has prompted an appreciation of the quality of life for survivors. Women treated for cancer identify gynecologic issues as a major concern for both general health and the negative impact on sexual function that follow the cancer diagnosis and subsequent treatment. Unfortunately, issues related to sexual health continue to be underappreciated. Although comprehensive cancer centers have adopted specialized centers for survivorship issues, including those involving sexual health, consultations are not widely available in most communities. We provide background information on female sexual health, examine the impact of cancer treatment on sexual function, and discuss some of the major sexual health issues of women who have received a cancer diagnosis and been subsequently treated.

Pharmacogenomics and sexuality: A vision.
Nappi RE, Domoney C
Climacteric. 2013 Aug;16 Suppl 1:25-30. doi: 10.3109/13697137.2013.806402.

Female sexual dysfunction (FSD) is multidimensional with a complex interplay of bio-psychosocial factors modulating the clinical expression of sexual symptoms and associated distress. During the entire reproductive lifespan, intra- and interpersonal experiences shape human neuroendocrine and neurovascular sexual pathways. These are dependent on genetic and epigenetic mechanisms, including acquired medical conditions. Understanding the genetic basis of FSD can help to determine clinical phenotypes of women and therefore postulate the most effective intervention according to biological, psychological or environmental determinants. However, there is a paucity of studies demonstrating a genetic contribution to FSD and a diverse modulation of innate and acquired factors on discrete domains of sexual response and distress. This is evident from menarche to menopause. Pharmacogenomics is still in its infancy in the field

of sexual medicine and most data regarding genetic polymorphisms of drug targets associated with susceptibility to sexual dysfunction have been obtained in males. Pharmacogenomics may be the future of medical practice in women with FSD and may guide an individualized approach by predicting both therapeutic effects at varying dosages of hormonal and non-hormonal agents, and disadvantageous side-effects and drug interactions.

Effects of long-term high dose testosterone administration on vaginal epithelium structure and estrogen receptor-α and -β expression of young women.

Baldassarre M, Giannone FA, Foschini MP, Battaglia C, Busacchi P, Venturoli S, Meriggiola MC

Int J Impot Res. 2013 Sep;25(5):172-7. doi: 10.1038/ijir.2013.9.
http://www.ncbi.nlm.nih.gov/pubmed/23552580

To date, the effects of long-term testosterone (T) administration on the human vagina are not completely understood. Thus, the aim of this study was to investigate the effects of long-term T treatment on vaginal tissue histology, estrogen receptor alpha (ERα) and beta (ERβ) expression and proliferation in female to male transsexual subjects (FtM). We compared vaginal samples from FtM subjects with those of premenopausal women (PrM) and postmenopausal women (M) not receiving any hormonal treatment for at least 2 years. Vaginal tissue samples from 16 FtM subjects treated with T (intramuscular injections of 100 mg Testoviron Depot/7-10 days for at least 1 year), undergoing sex reassignment surgery, and 16 PrM and 16 M subjects undergoing a vaginal hysterectomy for prolapse, were collected. For each sample, morphology, glycogen content, proliferation (ki-67), ERα and ERβ expression were evaluated. Vaginal samples from FtM showed a loss of normal architecture of the epithelium, intermediate and superficial layers were completely lost, and glycogen content was depleted. T administration resulted in a strong proliferation reduction when compared with both M and PrM subjects. Stromal and epithelial ERα as well as ERβ were significantly decreased in FtM when compared with PrM subjects. In conclusion, our data suggests that systemic T administration at supraphysiological dosage, determines profound changes in histomorphology and reduces ERs expression and proliferation of vaginal epithelium.