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This newsletter is quarterly and contains abstracts from medical journals published between June and December 2011. Abstracts presented at scientific meetings are also included. Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia / Vulvovaginal Pain

Prevalence and demographic characteristics of vulvodynia in a population-based sample.

Reed BD, Harlow SD, Sen A, Legocki LJ, Edwards RM, Arato N, Haefner HK

Am J Obstet Gynecol. 2011 Aug 22. [Epub ahead of print]

OBJECTIVE: The objective of the study was to determine the prevalence and characteristics of vulvodynia among women in southeast Michigan. **STUDY DESIGN:** A population-based study of adult women was conducted, using telephone recruitment and completion of a self-administered survey. Weighted estimates of vulvodynia prevalence and characteristics were determined. **RESULTS:** Over a year, 2542 women were recruited and 2269 (89.3%) completed the self-administered survey. The weighted prevalence of vulvodynia was 8.3% (95% confidence interval, 7.0-9.8) or approximately 101,000 women in the targeted population. Prevalence remained stable through age 70 years and declined thereafter. Among sexually active women, the prevalence was similar at all ages. Of 208 women meeting vulvodynia criteria, 101 (48.6%) had sought treatment, and only 3 (1.4%) had been diagnosed with vulvodynia (unweighted values). Previous vulvodynia symptoms had resolved in 384 women (16.9%) after a mean duration of 12.5 years. **CONCLUSION:** Vulvodynia is common, although rarely diagnosed. Prevalence remains high among sexually active women of any age.

Age of sexual debut and central introital dyspareunia.

Donders GG, Folens S, Peperstraete B, Bellen G

Eur J Obstet Gynecol Reprod Biol. 2011 Sep;158(1):90-2.

OBJECTIVES: Analysis of characteristics of patients with introital central dyspareunia. Is late coitarche (age at first sexual intercourse) a risk factor for introital dyspareunia? **STUDY DESIGN:**

145 women attending a vulvo-vaginitis clinic in secondary and tertiary care center in Tienen and Leuven, Belgium, with central introital pain during sexual intercourse. RESULTS: The mean age of the study group was 32 years, and 5% were 60 years of age or older. Of the patients, 51% had primary and 49% secondary dyspareunia. Before referral, two-thirds of the patients had already tried several types of therapy, including psychiatric help in 16% of cases. The study group of patients with central introital dyspareunia had a coitarche at a mean of 18.3 years. 72% of the dyspareunic women with coitarche later than 18 had to regularly interrupt intercourse because of pain, compared with 52% of women with coitarche before 18 ($p < 0.05$). A strong correlation was found between the age of sexual debut and the necessity to interrupt intercourse attempts due to pain ($p < 0.001$). Frequency of intercourse was also found to be inversely related to coitarche. CONCLUSION: Women with introital dyspareunia had their sexual debut at a later age than otherwise comparable women. Late coitarche is inversely related to frequency of attempted intercourse and to the necessity to interrupt intercourse due to pain, suggesting a relation between coitarchal age and severity of dyspareunia. A possible explanation is increased fibrosis and stiffening of the hymenal remnants at the posterior vulvar commissural due to increasing age in primary, and repeated injury by sexual contacts in secondary, central introital dyspareunia patients.

Repeated vulvovaginal fungal infections cause persistent pain in a mouse model of vulvodynia.

Farmer MA, Taylor AM, Bailey AL, Tuttle AH, MacIntyre LC, Milagrosa ZE, Crissman HP, Bennett GJ, Ribeiro-da-Silva A, Binik YM, Mogil JS
Sci Transl Med. 2011 Sep 21;3(101):101ra91.

Provoked vestibulodynia, the most common form of vulvodynia (unexplained pain of the vulva), is a prevalent, idiopathic pain disorder associated with a history of recurrent candidiasis (yeast infections). It is characterized by vulvar allodynia (painful hypersensitivity to touch) and hyperinnervation. We tested whether repeated, localized exposure of the vulva to a common fungal pathogen can lead to the development of chronic pain. A subset of female mice subjected to recurrent *Candida albicans* infection developed mechanical allodynia localized to the vulva. The mice with allodynia also exhibited hyperinnervation with peptidergic nociceptor and sympathetic fibers (as indicated by increased protein gene product 9.5, calcitonin gene-related peptide, and vesicular monoamine transporter 2 immunoreactivity in the vaginal epithelium). Long-lasting behavioral allodynia in a subset of mice was also observed after a single, extended *Candida* infection, as well as after repeated vulvar (but not hind paw) inflammation induced with zymosan, a mixture of fungal antigens. The hypersensitivity and hyperinnervation were both present at least 3 weeks after the resolution of infection and inflammation. Our data show that infection can cause persistent pain long after its resolution and that recurrent yeast infection replicates important features of human provoked vulvodynia in the mouse.

Vulvodynia interventions--systematic review and evidence grading.

Andrews JC

Obstet Gynecol Surv. 2011 May;66(5):299-315.

INTRODUCTION: State of the art guidance exists for management of vulvodynia, but the scientific basis for interventions has not been well described. Although there are many interventional therapies, and their use is increasing, there is also uncertainty or controversy about their efficacy. **OBJECTIVE:** To systematically assess benefits and harms of interventional therapies for vulvodynia and vestibulodynia. **METHODS:** The following databases were searched, using MeSH terms for studies related to the treatment of vulvodynia or vulva pain/pruritus/dysesthesia/hyperesthesia/hypersensitivity: MEDLINE, PsycINFO, Scopus, Cochrane Library, EBSCO Academic, and Google Scholar. Using Medical Subject Reference sections of relevant original articles, reviews, and evidence-based guidelines were screened manually. Manual searching for indirect evidence supporting interventions was done whenever no direct evidence was found for a treatment described within a review or guideline. Each modality is assessed with a grading system similar to the Grades of Recommendation, Assessment, Development, and Evaluation system. The grading system assesses study quality, effect size, benefits, risks, burdens, and costs. **RESULTS:** For improvement of pain and/or function in women with vestibulodynia (provoked localized vulvodynia), there was fair evidence that vestibulectomy was of benefit, but the size of the effect cannot be determined with confidence. There was good evidence of a placebo effect from multiple studies of nonsurgical interventions. There was fair evidence of lack of efficacy for several nonsurgical interventions. There were several interventions for which there were insufficient evidence to reliably evaluate. There was insufficient evidence to judge harms or to judge long-term benefits. For clinically meaningful improvement of pain in women with generalized unprovoked vulvodynia, there was insufficient evidence for benefit of any intervention. There was fair evidence of a placebo effect in people with neuropathic pain and functional pain syndromes, from multiple studies of interventions. Based on indirect evidences from studies of patients with other pain disorders, interventions may be selected for future research. **CONCLUSION:** There is fair evidence for effectiveness of vestibulectomy for vestibulodynia; however, there is uncertainty about the size of the absolute effect, because of the risk of bias inherent in studies of pain interventions without a placebo control group. Providers and patients looking for evidence-based interventions for generalized unprovoked vulvodynia may need to rely on indirect evidences from studies of neuropathic pain and functional pain syndromes. **TARGET AUDIENCE:** Obstetricians & gynecologists, family physicians. **LEARNING OBJECTIVES:** After completion of this educational activity, the obstetrician/gynecologist should be better able to identify potential causes of vulvar pain to facilitate diagnosis of vulvodynia and vestibulodynia, distinguish between the symptoms of localized, provoked vulvodynia and generalized unprovoked vulvodynia to select the most appropriate therapies, evaluate the efficacy of surgical and nonsurgical interventions for the treatment of generalized unprovoked and localized, provoked vulvodynia. In addition, assess the benefits and risks of interventional therapies for vulvodynia and vestibulodynia to improve patient care.

Long-term follow up of posterior vestibulectomy for treating vulvar vestibulitis.

Tommola P, Unkila-Kallio L, Paavonen J

Acta Obstet Gynecol Scand. 2011 Nov;90(11):1225-31. doi: 10.1111/j.1600-0412.2011.01248.x.

OBJECTIVE: To evaluate the safety and the effectiveness of posterior vestibulectomy in the treatment of vulvar vestibulitis syndrome. **DESIGN:** A retrospective cohort study. **SETTING:** University Hospital, tertiary referral center. **POPULATION:** Seventy women treated by posterior vestibulectomy for severe vulvar vestibulitis syndrome during 1995-2007 at the Department of Obstetrics and Gynecology, University Hospital, Helsinki. **METHODS:** All operated women were invited to a long-term follow-up study. Patient characteristics, baseline visual analog scale (VAS) for dyspareunia and data from the postoperative period were collected. Of the 70 women, 57 attended the follow-up visit including face-to-face interview, gynecological examination with swab-touch test for vestibular tenderness, current VAS score for dyspareunia and McCoy questionnaire for sexual problems. **MAIN OUTCOME MEASURES:** Short-term and long-term complication rates, dyspareunia by VAS score, vestibular tenderness, sexual problem index and overall patient satisfaction. **RESULTS:** Ninety-one per cent were satisfied with the outcome. The VAS for dyspareunia decreased from a median of 9 to 3 (66.7% decrease; $p < 0.001$). Posterior vestibular tenderness was absent in 34 patients (64.2%). Six (8.6%) patients developed postoperative bleeding and 11 (15.7%) mild wound infection. Bartholin's cysts occurred in four (5.7%) patients. **CONCLUSIONS:** Posterior vestibulectomy is effective and safe in the treatment of severe vulvar vestibulitis syndrome and provides long-term patient satisfaction.

Vaginal diazepam use with urogenital pain/pelvic floor dysfunction: serum diazepam levels and efficacy data.

Carrico DJ, Peters KM

Urol Nurs. 2011 Sep-Oct;31(5):279-84, 299.

Vaginal diazepam is used off-label for pelvic floor dysfunction and urogenital pain, but serum levels with efficacy have not been reported until now. One clinician evaluated 21 women for overall, levator, and vulvar pain pre- and one-month post-daily diazepam treatment. One-month post-treatment assessments and serum diazepam levels were done; 62% were moderately or markedly improved. Levator examination pain scores were significantly improved, and vulvar pain scores decreased post-treatment. Serum diazepam levels were within normal limits. Vaginal diazepam may be helpful in treating pelvic floor/urogenital pain conditions.

Vulvar pain syndromes: Making the correct diagnosis.

Edwards L, Gunter J, Haefner HK

OBG Management. Vol 23, No. 9. September 2011

No abstract available.

Full text available online: http://www.obgmanagement.com/article_pages.asp?AID=9876&UID

Vulvar pain syndromes: A bounty of treatments—but not all of them are proven.

Edwards L, Gunter J, Haefner HK

OBG Management. Vol 23, No. 10. October 2011

No abstract available.

Full text available online: http://www.obgmanagement.com/article_pages.asp?AID=9943

Vulvar pain syndromes: Causes and treatment of vestibulodynia.

Edwards L, Gunter J, Haefner HK

OBG Management. Vol 23, No. 11. November 2011

No abstract available.

Full text available online: http://www.obgmanagement.com/article_pages.asp?AID=10036

Real time 4D ultrasonography measurements of the pelvic floor muscles in women with and without Provoked Vestibulodynia.

Morin M, Bergeron S, Khalife S, Binik Y, Mayrand MH

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

Autonomic testing for small fiber neuropathies in vulvodynia patients.

Harris D, Coady D, Robinson-Papp J

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

Provoked Vestibulodynia – predictors and evaluation of treatment outcome.

Heddini U, Johannesson U, Nilsson KW, Bohm-Starke N

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

Long-term well-being after surgical or conservative treatment of severe vulvar vestibulitis.

Tommola P, Unkila-Kallio L, Paavonen J

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Enoxaparin for Localized Provoked Vulvodynia: A randomized double blind placebo controlled study.

Farajun Y, Zarfati D, Abramov L, Bornstein J

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Proteomic studies identify novel proteins in the vestibule that are characteristic of Vulvodynia.

MacNeill C, Phelps D, Umstead T, Carrillo MA, Gupta M, Floros J

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Experience of symptoms, sexual function and attitudes toward counseling of women with newly diagnosed Vulvodynia.

Piper CK, Legocki L, Reed B, Moravek M, Lavin K, Wade K, Musolf K, Haefner HK

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Gene expression analysis reveals altered immuno-inflammatory response in patients with Provoked Vulvodynia.

Breshears LM, Peterson ML, Harlow BL

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgt/toc/2011/10001>.

A novel genetic association for primary severe Localized Provoked Vulvodynia.

Falik Zaccai TC, Kalfon L, Azran A, Farajun Y, Tubin E, Hemo O, Abramov L, Yeshaya A, Bornstein J

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgt/toc/2011/10001>.

Does sexual abuse and physical abuse predict treatment response in Vestibulodynia?

Foster DC, Poleshuck EL

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgt/toc/2011/10001>.

Childhood urogenital hypersensitivity among adult women with and without Vulvodynia.

Legocki L, Edwards RM, Harlow SD, Sen A, Haefner HK, Reed BD

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgt/toc/2011/10001>.

Psychological characteristics and predictors for outcome of randomized, double blinded botox study on women with Vestibulodynia.

Petersen CD, Giraldi A, Lundvall L, Kristensen E

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

The use of topical amitriptyline cream in the management of Vestibulodynia.

Pagano R, Wong S

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Safety and efficacy of human fibroblast lysate cream for Provoked Localized Vulvodynia.

Donders GG, Bellen G, Fiewis S

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Vulvodynia and other chronic pain comorbidities.

Reed BD, Harlow SD, Legocki LJ, Edwards RM, Sen A, Haefner HK

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Erosive Vulvovaginal Lichen Planus and Vulvodynia: an association?

Coombs A, Edwards L

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Effect of palmitoylethanolamide polidatin combination in patients with Vestibulodynia treated with transcutaneous electrical nerve stimulation (TENS) therapy: a randomized double blind-controlled trial.

Murina F, Graziottin A, Felice R, Radici G, Tognocchi C

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

A community-based study of risk factors for Vulvodynia using administrative health care records.

Harlow BL, Oakes JM, Nguyen R, MacLehose SS, Brady SS, Breshears L, Peterson M

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Urinary and sexual discomfort assessment in Vulvodynia: a case-control study.

Belfiore P, Amico ML, Puccio G, Lupi M, Gugliotta G

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Characterizing and comparing pelvic floor muscle function in women with Provoked Vestibulodynia using a dynamometric speculum: a controlled study.

Morin M, Bergeron S, Khalife S, Binik Y, Dupuis MJ, Bourbonnais D

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/jlgtd/toc/2011/10001>.

Unprovoked Localized Vestibulodynia in late estrogen-deplete menopause – a case series.

Goetsch MF

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

Treatment outcomes of physical therapy for Vestibulodynia: an international case series.

Hartmann D

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

The relationship between hip disorders and chronic pelvic pain.

Coady DJ, Futterman SJ, Shah M, Coleman S

Abstract presented at the XXI World Congress of the International Society for the Study of Vulvovaginal Disease: Sept 2011.

Abstract is printed in the Journal of Lower Genital Tract Disease October 2011 Supplement (Vol 15, Issue 5) available online: <http://journals.lww.com/ilgtd/toc/2011/10001>.

Effect of transcutaneous electrical nerve stimulation on the postpartum dyspareunia treatment.

Dionisi B, Senatori R

J Obstet Gynaecol Res. 2011 Jul;37(7):750-3. doi: 10.1111/j.1447-0756.2010.01425.x. [Epub 2011 Mar 13]

AIM: This article will evaluate the safety and efficacy of intravaginal transcutaneous electrical nerve stimulation (TENS) for the treatment of vulvar pain and dyspareunia during the postpartum period related to perineal trauma caused by episiotomy. METHODS: From January 2007 to January 2009, 45 women presenting with postpartum dyspareunia related to perineal trauma after a vaginal delivery were educated on the importance of the pelvic floor and its part in continuing dyspareunia. The treatment consisted of weekly applications of intravaginal TENS in an outpatient setting and daily home therapy with myofascial stretching and exercises of the pelvic floor musculature. The results were evaluated using the cotton swab test, the Marinoff Dyspareunia Scale and the Visual Analog Scale, and the anovulvar distance was assessed prior to and at the end of the treatment period. RESULTS: Of the women included in the study,

84.5% reported an improvement of dyspareunia after only five applications of TENS, with a total remission of symptoms (in 95% of patients) at the end of the protocol. At follow-up, eight months after the end of treatment, all patients were pain free. **CONCLUSIONS:** Therapy with intravaginal transcutaneous nerve stimulation and pelvic floor relaxation exercises is safe and effective in the improvement of vulvar pain and dyspareunia in women with postpartum perineal trauma due to episiorrhaphy, after spontaneous delivery.

Origins of Western diseases.

Quinn M

J R Soc Med. 2011 Nov;104(11):449-56.

Recent gynaecological studies show that childbirth, constipation, trauma and surgery cause injuries to autonomic nerves at different anatomical sites in the female pelvis resulting in endometriosis, adenomyosis and fibroids. Re-growth of abnormal nerves causes allodynic symptoms ('light touch causing pain or discomfort') some years later including vulvodynia, dyspareunia, dysmenorrhea, irritative bladder and bowel symptoms. Further consequences of autonomic denervation include tissue hypoplasia and hyperplasia, visceral dysfunction, susceptibility to infection, alcohol, tobacco and drugs, as well as pain with sensitization of the central nervous system. The 'autonomic denervation' view extrapolates these observations from the female pelvis to the varied anatomy of branches of the cardiac and coeliac plexi to provide primary mechanisms for many forms of Western disease. This account sets out the autonomic denervation view, identifies features of autonomic denervation in extrapelvic organs, and, contrasts it with prior accounts of chronic Western diseases including those of DP Burkitt, PRJ Burch and DP Barker.

Characteristics of the pain observed in the focal vulvodynia syndrome (VVS).

Donders G, Bellen G

Med Hypotheses.2011 Oct 29. [Epub ahead of print]

Symptoms and signs of patients with focal vulvodynia or vulvo-vestibulitis syndrome (VVS) are variable in location and severity. It is not known whether the location of the most severe pain in the vestibulum is linked to the complaints and perhaps a different entity. A clinical gut feeling suggests that two distinct varieties of focal vulvodynia may be either focused at 2 points (5 and 7 o' clock) or at 4 points (5, 7, 1 and 11 o' clock). A questionnaire was filled out by 30 women with focal vulvodynia during 147 visits and checked for completeness by an independent study nurse. Another investigator evaluated the clinical signs of VVS, blinded to the patients history or complaints. The visual analogue score (VAS) of pain experienced upon attempt of sexual contact was used as a marker of severity. Focal vulvar pain was assessed using Q-tip with a score from 1 to 10 on 7 areas of the vestibulum. Besides pain during sexual contact, 47% also had pain on inserting a tampon. More than 40% of women suffer since more than 3years, 70% had to interrupt the act of sexual intercourse mostly or always due to unbearable pain and 25% never had satisfactory sex due to this pain. Feeling deep pain, burning lasting for 12-24h after

sexual contact, and stopping the attempt of intercourse were more prominent in women with high pain scores (VAS): 26% of women with VAS >7 had no sex during the last year versus 6% in the group with low pain score (p=0.004). Patients suffering from para-urethral pain zones at 1 and 11 o' clock, have more often pain upon deep penetration, and experienced more pain when inserting tampons than patients with only painful areas at 5 and 7 o' clock (p=0.001). We conclude that patients with severe disease display a different panel of complaints than women with less pain. Patients with focal pain at 1 and 11 o' clock have more deep pain sensations, but feel less pain during insertion of tampons. Hence disease with bi-focal disease may have a different ethiopathogenesis than 4-focal disease. Glands of Bartholin and Skene may be involved in this pathogenesis.

Bladder pain syndrome/interstitial cystitis: a reappraisal for the clinician.

Mahmoud MS

J Reprod Med.2011 Sep-Oct;56(9-10):405-9.

Bladder pain syndrome--formally known as interstitial cystitis--is a chronic bladder disorder characterized by pelvic pain and urinary irritability symptoms. The physiopathology is still unclear but is thought to involve bladder mucosal injury, inflammation and neurologic dysfunction. It is hard to diagnose this entity due to symptoms that are common to several other pathologies such as chronic pelvic pain, endometriosis, overactive bladder, urinary tract infection, and vulvodynia, and due to the lack of specific findings. A combination of history, physical examination, and diagnostic tools helps the establishment of the diagnosis by ruling out other similar pathologies. Treatment is multimodal and combines behavioral changes, drugs administered orally or intravesically and even surgery for refractory cases.

[In process citation] [Article in French].

Bazin S, Lefebvre J, Fortier M, Brisson J, Brouillette F, Bujold E, Bouchard C

J Obstet Gynaecol Can. 2011 Aug;33(8):838-43.

OBJECTIVE: Our objective was to assess the short-term effect of an estrogen cream on symptoms associated with provoked vestibulodynia. **METHODS:** We undertook a double-blind randomized trial in women who had experienced dyspareunia satisfying the Friedrich criteria for at least three months. We compared the daily application of 3 g of vaginal cream containing 1.875 g of conjugated estrogens for six weeks (estrogen group) with the application of a comparable cream without estrogens (placebo group). The main outcome was modification of dyspareunia, determined by a visual analogue scale of pain from the pretreatment period to the post-treatment period. Secondary outcomes were colposcopic evaluation of the vulva and pain reported during the swab test. **RESULTS:** Of 69 women randomized, 61 participated for the full duration of the trial. Dyspareunia was significantly lessened in both groups (estrogen group: 7.4 ± 1.9 pre-treatment vs. 4.8 ± 3.0 post-treatment, $P < 0.01$; placebo group: 7.1 ± 1.9 vs. 4.9 ± 2.7 , $P < 0.01$), but the difference observed in terms of decrease between the two groups was not found to be significant ($P = 0.5$). Alternatively, the group treated with estrogen

cream showed (1) a more substantial decrease of the pain reported at the orifices of the Bartholin's glands when palpated with a swab ($P < 0.01$), and (2) a decrease of the inflammation observed at the orifices of the Bartholin's glands orifices and the posterior fourchette ($P < 0.01$). **CONCLUSION:** Applying a vaginal cream, whether it contains estrogens or not, for six weeks lessens dyspareunia. Adding estrogens to such a cream could facilitate a decrease of the inflammation observed at the orifices of the Bartholin's glands and the vestibule.

The relationship between female sexual arousal and response bias in women with and without Provoked Vestibulodynia.

Boyer SC, Pukall CF, Holden RR

J Sex Res. 2011 Aug 15. [Epub ahead of print]

Smaller correlations have typically been found between genital and subjective sexual arousal in female versus male samples. This study evaluated the association between response bias and the relationship between genital and subjective arousal (i.e., concordance) in women with ($n = 20$) and without ($n = 21$) provoked vestibulodynia. Participants ($M = 21.27$ years, $SD = 2.27$) underwent blood flow imaging via a laser Doppler imager to assess genital responsiveness to a visual erotic stimulus; subjective arousal was assessed during and following the film. The relationships between three types of subjective arousal ratings (perceived sexual arousal, perceived genital responsiveness, and reported desire to engage in sexual activity) and two forms of socially desirable responding (impression management and self-deceptive enhancement) were examined. Concordance estimates were statistically non-significant in both groups, with the exception of the desire to engage in sexual activity, which was moderately correlated with genital arousal in the control group. Impression management was not a statistically significant moderator of the relationship between genital and subjective arousal, but was moderately negatively related to the three forms of subjective arousal ratings in the provoked vestibulodynia group. The results highlight the importance of assessing response bias in laboratory studies comparing women with and without sexual dysfunction.

The influence of depression and anxiety on risk of adult onset vulvodynia.

Khandker M, Brady SS, Vitonis AF, Maclehose RF, Stewart EG, Harlow BL

J Womens Health (Larchmt). 2011 Oct;20(10):1445-51.

BACKGROUND: Studies have shown that women with vulvodynia are more psychologically distressed than women without vulvodynia. These studies, however, have not effectively established temporal associations between diagnosed psychiatric disorders and vulvodynia. **METHODS:** The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) was administered to 240 case-control pairs of women with and without vulvodynia. Interviews established age at first onset of diagnosed mood and anxiety disorder. Age information was used to determine whether the first episode of mood and/or anxiety was antecedent or subsequent to the first onset of vulvodynia symptoms. Conditional logistic regressions tested whether antecedent depression or anxiety was more likely among women with or without

vulvodynia. Cox proportional hazards modeling was then used to estimate risk of subsequent new or recurrent onset of mood or anxiety disorder. RESULTS: After adjusting for education, race, age at menarche, age at first tampon use, and age at first sexual intercourse, odds of vulvodynia were four-times more likely among women with antecedent mood or anxiety compared to women without (95% confidence interval [CI] 2.1-7.5). Vulvodynia was associated with new or recurrent onset of mood or anxiety disorder after adjustment (hazard ratio [HR] 1.7, 95% CI 1.1-2.6) and did not significantly change after including history of mood or anxiety disorder before the onset of vulvodynia or reference age of controls in the models. CONCLUSIONS: This is the first community-based epidemiologic study demonstrating that DSM-IV-diagnosed antecedent depression and anxiety disorders influence the risk of vulvodynia and that vulvodynia increases the risk of both new and recurrent onset of psychopathology.

Comment in J Womens Health (Larchmt). 2011 Oct;20(10):1433.

One women's voice for all.

Goldstein I

J Sex Med. 2011 Jun;8(6):1553-4. doi: 10.1111/j.1743-6109.2011.02302.x.

No abstract available.

The Journal of Sexual Medicine: sexual pain leader or vulvar disorder follower.

Goldstein I

J Sex Med. 2011 Oct;8(10):2663-5. doi: 10.1111/j.1743-6109.2011.02475.x.

No abstract available.

Management of female sexual pain disorders.

Boyer SC, Goldfinger C, Thibault-Gagnon S, Pukall CF

Adv Psychosom Med. 2011;31:83-104.

Our understanding of the sexual pain disorders vaginismus and dyspareunia has been fundamentally altered over the past two decades due to increased attention and empirically sound research in this domain. This increased knowledge base has included a shift from a dualistic view of the etiology of painful and/or difficult vaginal penetration being due to either psychological or physiological causes, to a multifactorial perspective. The present chapter reviews current classification and prevalence rates, including ongoing definitional debates. Research regarding the etiology, assessment and management of sexual pain disorders is discussed from a biopsychosocial perspective. Cyclical theories of the development and maintenance of sexual pain disorders, which highlight the complex interplay among physiological, psychological and social factors, are described. Medical/surgical treatment options, pelvic floor rehabilitation and psychological approaches are reviewed, as well as future directions in treatment research.

To lube or not to lube: Experiences and perceptions of lubricant use in women with and without dyspareunia.

Sutton KS, Boyer SC, Goldfinger C, Ezer P, Pukall CF

J Sex Med. 2011 Nov 14. doi: 10.1111/j.1743-6109.2011.02543.x. [Epub ahead of print]

INTRODUCTION: There are few studies examining the relationship between lubricant use and sexual functioning, and no studies have examined this relationship in women with dyspareunia. Vaginal dryness is a prevalent complaint among women of all ages. There is an association between vaginal dryness and painful intercourse; therefore, women with dyspareunia represent a particularly relevant sample of women in which to investigate lubricant use. **AIM:** The aim of this study was to examine differences between women with and without dyspareunia in self-reported natural lubrication and attitudes toward and use of personal lubricants. **METHODS:** Respondents completed an online survey including questions on demographics, gynecological/medical history, sexual functioning, and lubricant use and attitudes. **MAIN OUTCOME MEASURES:** The main outcome measures used were the Female Sexual Function Index (FSFI) and questions regarding attitudes toward and use of lubricants. **Results.** Controls scored higher on the lubrication subscale of the FSFI than women with dyspareunia ($P < 0.001$). Women with dyspareunia reported greater frequency of lubricant use during sexual activity over the last year ($P < 0.01$). They were also more likely to use lubricant prior to penetration ($P < 0.05$). The most common use for controls was to enhance sexual experiences. This was also a common answer for women with dyspareunia; however, in this group, the most common reason was to reduce/alleviate pain. Lubricants were rated as less effective among women with dyspareunia vs. controls across all reported reasons for use. Nevertheless, lubricant use was still rated as being moderately effective in alleviating pain for women with dyspareunia. **CONCLUSION:** Women with dyspareunia have more difficulty with natural lubrication; it is consequently not surprising that they reported using lubricant more frequently than control women. Women with dyspareunia reported using lubricants more often than controls to try to prevent or alleviate pain and reported this as being a moderately effective strategy, suggesting that it may be a useful tool for some women with dyspareunia.

Psycho emotional impact of women with provoked vestibulodynia.

Ventolini G, Balasko B

Minerva Psichiatrica. 2011 June;52(2):97-9.

AIM: To assess the psycho emotional impact of women with provoked vestibulodynia we invited patients to respond to the Brief Symptom Inventory (BSI). We evaluated psychopathological differences between patients who improved and the ones who did not improve to a standard protocol for provoked vestibulodynia management (PVM). **METHODS:** The study received IRB approval and took place at a university private practice referral center for vulvovaginal conditions. The patients were randomly selected. There were 74 patients included in this cohort study using a standardized protocol for PVM. The patients completed the BSI. The evaluators of the BSI were blinded to the patient's PVM outcomes. Twenty four patients were randomly selected. Twenty two agreed to participate and were

divided into 2 groups: A: 12 patients who improved with the PVM protocol and B: 10 patients who did not improve with the PVM protocol. RESULTS: Regarding the BSI subscales, patients from group A were less likely to show psychopathological burden than those from group B (P=0.001). Specifically patients from group B demonstrated an increase in depression, anxiety, hostility and psychoticism subscale scores compared to group A. The global severity index was also increased in group B compared to group A. (P=0.01) .The subscales scores of somatization, obsessive compulsion and sensitivity were comparable in the 2 groups (P=0.35). CONCLUSION: Patients with provoked vulvodynia who improved their condition following a standardized management protocol showed less psychological distress scores as measured by the BSI compared to the group who did not improve clinically.

De novo pudendal neuropathy after TOT-O surgery for stress urinary incontinence.

Paulson JD, Baker J

JSLs. 2011 Jul-Sep;15(3):326-30.

BACKGROUND AND OBJECTIVES: Five cases of pelvic nerve complications after transobturator tape (TOT) inside-out surgical procedures for stress urinary incontinence are presented.

METHODS: We conducted a chart review of patients with complications referred to our practice.

RESULTS: Five patients with nerve complications after TOT inside-out procedures were investigated. Pudendal neuropathy and interstitial cystitis were seen in this series of patients with several patients having myofascial pain in the lower abdominal area.

CONCLUSIONS: Although not commonly reported, complications from needle placement and from the area of needle exit in a TOT procedure can exist, and the surgeon must be careful when placing the needle through the area of the obturator fossa.

Pudendal neuralgia following transobturator inside-out tape procedure (TVT-O)-case report and anatomical study.

Masata J, Hubka P, Martan A

Int Urogynecol J. 2011 Sep 2. [Epub ahead of print]

Persistent pain after TVT-O procedure is a rare complication. Nerve injuries have been suspected as a cause of persistent pain. We present one case of atypical postoperative pain-pudendal neuralgia following TVT-O procedure-which persisted 3 years after the primary procedure. The patient required surgical removal of the tape, which brought only partial relief. Complete relief from pain was afterwards achieved with repeated local applications of anesthetics with corticosteroids. The recurrent stress urinary incontinence was treated with retropubic TVT. Pudendal nerve irritation was also described after retropubic sling procedure, and the cadaveric dissection indicated the theoretic possibility of nerve injury during retropubic sling procedure. To explain the mechanism of nerve injury, we performed cadaveric dissections on a formalin-embalmed female body. We were able to demonstrate the contact of the needle with the pudendal nerve after aberrant passage of the inserter.

Women's bike seats: A pressing matter for competitive female cyclists.

Guess MK, Partin SN, Schrader S, Lowe B, Lacombe J, Reutman S, Wang A, Toennis C, Melman A, Mikhail M, Connell KA

J Sex Med. 2011 Nov;8(11):3144-3153. doi: 10.1111/j.1743-6109.2011.02437.x.

INTRODUCTION: There are numerous genital complaints in women cyclists, including pain, numbness, and edema of pelvic floor structures. Debate ensues about the best saddle design for protection of the pelvic floor. **AIM:** To investigate the relationships between saddle design, seat pressures, and genital nerve function in female, competitive cyclists. **Methods.** We previously compared genital sensation in healthy, premenopausal, competitive women bicyclists and runners. The 48 cyclists from our original study comprise the study group in this subanalysis. **Main Outcome Measures.** **MAIN OUTCOME MEASURES:** (i) genital vibratory thresholds (VTs) determined using the Medoc Vibratory Sensation Analyzer 3000 and (ii) saddle pressures as determined using a specially designed map sensor. **Results.** More than half of the participants (54.8%) used traditional saddles, and the remainder (45.2%) rode with cut-out saddles. On bivariate analysis, use of traditional saddles was associated with lower mean perineal saddle pressures (MPSP) than riding on cut-out saddles. Peak perineal saddle pressures (PPSP) were also lower; however, the difference did not reach statistical significance. Saddle design did not affect mean or peak total saddle pressures (MTSP, PTSP). Saddle width was significantly associated with PPSP, MTSP, and PTSP but not with MPSP. Women riding cut-out saddles had, on average, a 4 and 11 kPa increase in MPSP and PPSP, respectively, compared with women using traditional saddles ($P = 0.008$ and $P = 0.010$), after adjustment for other variables. Use of wider saddles was associated with lower PPSP and MTSP after adjustment. Although an inverse correlation was seen between saddle pressures and VTs on bivariate analysis, these differences were not significant after adjusting for age. **Conclusion.** Cut-out and narrower saddles negatively affect saddle pressures in female cyclists. Effects of saddle design on pudendal nerve sensory function were not apparent in this cross-sectional analysis. Longitudinal studies evaluating the long-term effects of saddle pressure on the integrity of the pudendal nerve, pelvic floor, and sexual function are warranted.

Nerve-stimulator-guided pudendal nerve block by pararectal approach.

Kim S, Song S, Paek O, Lee H, Park D, Lee J

Colorectal Dis. 2011 Jul 13. doi: 10.1111/j.1463-1318.2011.02720.x. [Epub ahead of print]

AIM: Various techniques have been described for performing a pudendal nerve block (PNB) and have associated problems such as multiple needle injections, the need for special equipment and consumption of time. This study aimed to describe a nerve-stimulator-guided PNB using a pararectal approach and to evaluate the safety and the efficacy of that procedure. **METHOD:** We conducted a prospective study of 53 patients who underwent a PNB from December 2009 to July 2010. With the index finger of the left hand inserted into anus, we guided the nerve stimulator needle along the 2nd finger tip on the ischial spine to the site where the maximal contraction of the external anal sphincter could be felt. Once the position of the needle tip had been confirmed, the desired drug was injected. Of the 53 patients, a cohort of 8

underwent manometry before and after the pudendal block. RESULTS: A total of 53 patients underwent the nerve-stimulator-guided procedure: 13 patients for pudendal neuralgia and the other 40 patients for anorectal disease. The mean maximal resting and squeezing pressures before the block were 55 and 161 mmHg, respectively, compared with 35 and 67 mmHg after the block. The PNB took just minutes to perform, was well tolerated by the patients, and resulted in neither severe complications nor repeated attempts. CONCLUSION: Nerve-stimulator-guided PNB using a pararectal approach proved to be easy and safe, with acceptable patient tolerance. In addition, it can be used for a variety of anorectal procedures where relaxation of anal tone is required.

Basic Science/Anatomy

Anatomic relationships of the pudendal nerve branches.

Montoya TI, Calver L, Carrick KS, Prats J, Corton MM
Am J Obstet Gynecol. 2011 Nov;205(5):504.e1-5.

OBJECTIVE: We sought to characterize the distribution of the pudendal nerve branches and to correlate findings with injury risk related to common midurethral sling procedures. STUDY DESIGN: Dissections were performed in 18 female cadavers. Biopsies were obtained to confirm gross findings by histology. RESULTS: In all dissections, most of the clitoral and perineal nerves coursed caudal to the ventral portion of the perineal membrane. The inferior rectal nerve did not enter the pudendal canal in 44% (n = 8) of specimens. Nerve tissue was confirmed histologically in tissue sampled. CONCLUSION: The clitoral and perineal branches of the pudendal nerve should be at low risk of direct nerve injury during midurethral slings and similar procedures as they course caudal to the ventral portion of the perineal membrane. The inferior rectal nerve might be at risk of injury during procedures that involve passage of needles through the ischioanal fossa.

Chemokine upregulation in response to anal sphincter and pudendal nerve injury: potential signals for stem cell homing.

Salcedo L, Sopko N, Jiang HH, Damaser M, Penn M, Zutshi M
Int J Colorectal Dis. 2011 Dec;26(12):1577-81.

PURPOSE: Stromal derived factor-1 (SDF-1) and monocyte chemotactic protein-3 (MCP-3) are signals forcing the migration of bone marrow-derived stem cells to ischemic tissue. This study investigates SDF-1 and MCP-3 expression following direct injury to the anal sphincter and pudendal nerve and to determine if these same mechanisms have any role. METHODS: Chemokine expression was studied after anal sphincter injury in female rats after either a sphincterotomy (n = 15), pudendal nerve crush (PNC; n = 15), sham pudendal nerve crush (n = 15), or acted as unmanipulated controls (n = 5). Analysis was done at 1 h and 10 and

21 days after injury. RESULTS: After injury, SDF-1 expression increased 40.2 ± 6.42 ($P = 0.01$) at 1 h and 28.2 ± 2.37 ($P = 0.01$) at 10 days, respectively, compared to controls. Likewise, MCP-3 expression increased 40.8 ± 8.17 ($P = 0.02$) at the same intervals compared to controls. After PNC, SDF-1 expression increased 46.4 ± 6.01 ($P = 0.02$) and 50.6 ± 10.11 ($P = 0.01$), and MCP-3 expression increased 46.3 ± 7.76 ($P = 0.03$) and 190.8 ± 22.15 ($P = 0.01$), respectively, at the same time intervals compared to controls. However, when PNC was compared to sham injured, a significant increase was seen in SDF-1 and MCP-3 at 10 days. At 21 days, PNC compared to sham injured was significantly low in expression for both SDF-1 and MCP-3 ($P < 0.05$). CONCLUSIONS: Direct anal sphincter injury results in higher levels of SDF-1 and MCP-3 expression soon after injury, whereas denervation via pudendal nerve crush results in greater SDF-1 and MCP-3 expression 10 days after injury. Chemokine overexpression suggests the potential for cell-based therapeutic strategies.

Topographical anatomy and desensitization of the pudendal nerve in adult male dromedary camels.

Ahmed AF, Al-Sobayil FA, Al-Halag MA
Theriogenology. 2011 Sep 1;76(4):772-7.

The objectives of this study were to describe the topographical anatomy of the pudendal nerve and to develop techniques of its blocking in adult male dromedary camels. Two cadavers and 30 adult male dromedary camels were used for the description of topographical anatomy and pudendal nerve block techniques, respectively. Results revealed that the pudendal nerve arises from the ventral branches of the 2nd and 3rd sacral spinal nerves. The nerve had three divisions; dorsal, middle, and ventral. The caudal rectal nerve was a branch of the dorsal division. Three blocking techniques were developed according to the results of topographical anatomy. The first technique was 15 cm cranial to the tail base and 7 cm lateral to the midline. The second was 12 cm cranial to the tail base and 7 cm lateral to the midline. The third was about 3 cm on either sides of the anus. Details and complications of each technique were reported. In conclusion, the anatomy of the pudendal nerve was different from that of cattle and horse. The second technique (12 cm cranial to the tail base and 7 cm lateral to the midline) for pudendal nerve block was superior among the three methods. Duration of nerve blocking was suitable for examination and for performing some surgical procedures in male dromedary camels.

Pain

Advancing a national agenda to eliminate disparities in pain care: Directions for health policy, education, practice, and research.

Meghani SH, Polomano RC, Tait TC, Vallerand AH, Anderson KO, Gallagher RM
Pain Medicine. Volume 12, Issue 11. Dec 2011. DOI: 10.1111/j.1526-4637.2011.01289.x

No abstract available.

Toward a better understanding and management of pain: A public health mandate.

Bachmann GA, Al-Najjar A
Journal of Women's Health. Vol. 20, No. 10, 2011. DOI: 10.1089/jwh.2011.3203

No abstract available.

Chronic pain, medical students, and primary care commentary on "what can we learn from first-year medical students' perception of pain in the primary care setting."

Norris TE
Pain Medicine. Vol 12, Issue 8, pages 1137-38. Aug 2011. DOI: 10.1111/j.1526-4637.2011.01194.x

No abstract available.

Learning from our learners: Implications for pain management education in medical schools.

Bair MJ
Pain Medicine. Vol 12, Issue 8, pages 1139-1141, August 2011. DOI: 10.1111/j.1526-4637.2011.01207.x

No abstract available.

A whole-person model of care for persistent pain: From conceptual framework to practical application.

Hayes C, Hodson FJ
Pain Medicine. Vol 12, Issue 12, pages 1738-1749. December 2011. doi: 10.1111/j.1526-4637.2011.01267.x

SETTING: The study was set in an Australian tertiary public hospital multidisciplinary pain center. OBJECTIVES: The objectives of the study were to describe the conceptual shift undertaken by a multidisciplinary team in moving from a traditional approach to an emerging paradigm in pain medicine and to describe the practical application of a whole-person model of

care and report outcomes over the period 2003–2010. DESIGN: The study design was descriptive, including a brief review of current evidence base, consideration of models of service delivery, and analysis of the impact of applying a new, whole-person model of care for persistent pain. INTERVENTION: Since 2004, a series of changes led to significant health system redesign. The process involved development of a broader, whole-person understanding of the individual with pain and a more integrated approach to service delivery across the spectrum from community to tertiary care. RESULTS: Broad trends in the period 2003–2010 included a modest reduction in referral rate, marked reduction in waiting times, more efficient staff utilization, inversion of the ratio of new assessments to review appointments, increased telephone contact with primary care, increased use of personalized pain management plans, reduced procedural interventions and increased attendance at and clinically significant gains from shorter and more flexible group programs. CONCLUSION: Changes to conceptual framework inevitably influence the practicalities of service delivery. The application of a whole-person model for persistent pain brought improved engagement with the individual in pain and more efficient delivery of care at a systems level.

Stigmatization of patients with chronic pain: The extinction of empathy.

Cohen M, Quintner J, Buchanan D, Nielsen M, Guy L

Pain Medicine. Vol 12, Issue 11, pages 1637-1643, Nov 2011. DOI: 10.1111/j.1526-4637.2011.01264.x

OBJECTIVE: To address how health professionals may inadvertently contribute to the stigmatization of patients with chronic pain. SETTING: Formulation and implementation of the Australian National Pain Strategy. DESIGN: Review of current concepts of stereotyping and stigma, consideration of their relationship to empathy, and how they might impinge upon the clinical encounter. FINDINGS: The extinction of empathy, which we refer to as “negative empathy,” can overwhelm health professionals, allowing the entry of negative community stereotypes of chronic pain sufferers and add to their stigmatization. Prevailing dualistic frames of reference encourage this process. CONCLUSION: Greater awareness by health professionals of their own potential, often inadvertent, contribution to the stigmatization of their patients with chronic pain may serve as a basis for an expanded model of clinical engagement.

Treatment of chronic non-cancer pain.

Turk DC, Wilson HD, Cahana A

The Lancet, Vol 377, Issue 9784, Pages 2226-2235, June 25, 2011 doi:10.1016/S0140-6736(11)60402-9

Chronic pain is a pervasive problem that affects the patient, their significant others, and society in many ways. The past decade has seen advances in our understanding of the mechanisms underlying pain and in the availability of technically advanced diagnostic procedures; however, the most notable therapeutic changes have not been the development of novel evidenced-based methods, but rather changing trends in applications and practices within the available

clinical armamentarium. We provide a general overview of empirical evidence for the most commonly used interventions in the management of chronic non-cancer pain, including pharmacological, interventional, physical, psychological, rehabilitative, and alternative modalities. Overall, currently available treatments provide modest improvements in pain and minimum improvements in physical and emotional functioning. The quality of evidence is mediocre and has not improved substantially during the past decade. There is a crucial need for assessment of combination treatments, identification of indicators of treatment response, and assessment of the benefit of matching of treatments to patient characteristics.

Effective treatment of chronic low back pain in humans reverses abnormal brain anatomy and function.

Seminowicz DA, Wideman TH, Naso L, Hatami-Khoroushahi Z, Fallatah S, Ware MA, Jarzem P, Bushnell MC, Shir Y, Ouellet JA, Stone LS
J Neurosci. 2011 May 18;31(20):7540-50.

Chronic pain is associated with reduced brain gray matter and impaired cognitive ability. In this longitudinal study, we assessed whether neuroanatomical and functional abnormalities were reversible and dependent on treatment outcomes. We acquired MRI scans from chronic low back pain (CLBP) patients before (n = 18) and 6 months after (spine surgery or facet joint injections; n = 14) treatment. In addition, we scanned 16 healthy controls, 10 of which returned 6 months after the first visit. We performed cortical thickness analysis on structural MRI scans, and subjects performed a cognitive task during the functional MRI. We compared patients and controls, as well as patients before versus after treatment. After treatment, patients had increased cortical thickness in the left dorsolateral prefrontal cortex (DLPFC), which was thinner before treatment compared with controls. Increased DLPFC thickness correlated with the reduction of both pain and physical disability. Additionally, increased thickness in primary motor cortex was associated specifically with reduced physical disability, and right anterior insula was associated specifically with reduced pain. Left DLPFC activity during an attention-demanding cognitive task was abnormal before treatment, but normalized following treatment. These data indicate that functional and structural brain abnormalities—specifically in the left DLPFC—are reversible, suggesting that treating chronic pain can restore normal brain function in humans.

Systematic review of tapentadol in chronic severe pain.

Riemsma R, Forbes C, Harker J, Worthy G, Misso K, Schäfer M, Kleijnen J, Stürzebecher S
Curr Med Res Opin. 2011 Oct;27(10):1907-30.

AIM: A systematic review of chronic pain treatment with strong opioids (step 3 WHO pain ladder) and a comparison to a new drug recently approved for the treatment of severe chronic pain in Europe, tapentadol (Palexia, Nucynta*), were performed.

METHODS: Thirteen electronic databases were searched as well as a number of other sources from 1980 up to November 2010 for relevant randomized controlled clinical trials in chronic

moderate and severe pain investigating at least one step 3 opioid. Chronic pain could be nociceptive or neuropathic, malignant or non-malignant, all systemic administrations were considered as well as trials of different lengths. Two separate analyses were performed, one only for trials which reported (at least as sub-groups) the outcome in patients with severe pain, the other including both moderate and severe pain conditions. With the exception of the direct comparison between tapentadol, oxycodone and placebo, indirect comparisons were performed based on a network analysis. Trials with an enriched or an enriched withdrawal design were excluded. Primary (pain intensity) and a number of secondary endpoints were evaluated, including pain relief (30% and 50%), patient global impression of change, quality of life, quality of sleep, discontinuations, as well as serious adverse events and selected adverse events. RESULTS: Only 10 trials were eligible for analysis of patients with severe pain (eight investigating tapentadol and two trials comparing buprenorphine patch vs placebo). For moderate and severe pain, 42 relevant trials were identified and indirect comparisons with transdermal buprenorphine, transdermal fentanyl, hydromorphone, morphine, and oxymorphone were performed. This report focuses on the network analysis. Tapentadol showed statistically favourable results over oxycodone for pain intensity, 30% and 50% pain relief, patient global impression of change (PGIC), and quality of life. Furthermore, some of the most important adverse events of chronic opioid treatment were significantly less frequent with tapentadol as compared to oxycodone, i.e. constipation, nausea, and vomiting; discontinuations due to these adverse events were found significantly reduced with tapentadol. Similar results were obtained for the network analysis, i.e. tapentadol was superior for the primary outcome (pain intensity) to hydromorphone and morphine, whereas fentanyl and oxymorphone showed trends in favour of these treatments. Significantly less frequent gastrointestinal adverse events of tapentadol were observed in comparison with fentanyl, hydromorphone, morphine, and oxymorphone, apparently leading to significantly reduced treatment discontinuations (for any reason). CONCLUSIONS: Taken together, the benefit-risk ratio of tapentadol appears to be improved compared to step 3 opioids.

Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch.

Anand P, Bley K

Br J Anaesth. 2011 Oct;107(4):490-502.

Topical capsaicin formulations are used for pain management. Safety and modest efficacy of low-concentration capsaicin formulations, which require repeated daily self-administration, are supported by meta-analyses of numerous studies. A high-concentration capsaicin 8% patch (Qutenza™) was recently approved in the EU and USA. A single 60-min application in patients with neuropathic pain produced effective pain relief for up to 12 weeks. Advantages of the high-concentration capsaicin patch include longer duration of effect, patient compliance, and low risk for systemic effects or drug-drug interactions. The mechanism of action of topical capsaicin has been ascribed to depletion of substance P. However, experimental and clinical studies show that depletion of substance P from nociceptors is only a correlate of capsaicin treatment and has little, if any, causative role in pain relief. Rather, topical capsaicin acts in the

skin to attenuate cutaneous hypersensitivity and reduce pain by a process best described as 'defunctionalization' of nociceptor fibres. Defunctionalization is due to a number of effects that include temporary loss of membrane potential, inability to transport neurotrophic factors leading to altered phenotype, and reversible retraction of epidermal and dermal nerve fibre terminals. Peripheral neuropathic hypersensitivity is mediated by diverse mechanisms, including altered expression of the capsaicin receptor TRPV1 or other key ion channels in affected or intact adjacent peripheral nociceptive nerve fibres, aberrant re-innervation, and collateral sprouting, all of which are defunctionalized by topical capsaicin. Evidence suggests that the utility of topical capsaicin may extend beyond painful peripheral neuropathies.

The development and psychometric validation of the Central Sensitization Inventory.

Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, Perez Y, Gatchel RJ
Pain Pract. 2011 Sep 27. doi: 10.1111/j.1533-2500.2011.00493.x. [Epub ahead of print]

Central sensitization (CS) has been proposed as a common pathophysiological mechanism to explain related syndromes for which no specific organic cause can be found. The term "central sensitivity syndrome (CSS)" has been proposed to describe these poorly understood disorders related to CS. The goal of this investigation was to develop the Central Sensitization Inventory (CSI), which identifies key symptoms associated with CSSs and quantifies the degree of these symptoms. The utility of the CSI, to differentiate among different types of chronic pain patients who presumably have different levels of CS impairment, was then evaluated. Study 1 demonstrated strong psychometric properties (test-retest reliability = 0.817; Cronbach's alpha = 0.879) of the CSI in a cohort of normative subjects. A factor analysis (including both normative and chronic pain subjects) yielded 4 major factors (all related to somatic and emotional symptoms), accounting for 53.4% of the variance in the dataset. In Study 2, the CSI was administered to 4 groups: fibromyalgia (FM); chronic widespread pain without FM; work-related regional chronic low back pain (CLBP); and normative control group. Analyses revealed that the patients with FM reported the highest CSI scores and the normative population the lowest ($P < 0.05$). Analyses also demonstrated that the prevalence of previously diagnosed CSSs and related disorders was highest in the FM group and lowest in the normative group ($P < 0.001$). Taken together, these 2 studies demonstrate the psychometric strength, clinical utility, and the initial construct validity of the CSI in evaluating CS-related clinical symptoms in chronic pain populations.

Acute and chronic pain: where we are and where we have to go.

Allegri M, Clark MR, De Andrés J, Jensen TS
Minerva Anestesiol. 2011 Nov 18. [Epub ahead of print]

In recent years, increasing attention has been focused on the treatment of acute and chronic pain with a considerable number of publications about it. Nevertheless all the attention focused on it, the evidence of pain treatments is still unfolding, and occasionally conflicting. Hence it is still necessary that we point out our research efforts in trying to obtain a better

understand of pathophysiology of pain and of real efficacy and safety of acute and chronic pain treatments. Our goal with this review is to summarize the latest research trends and the most advanced therapeutic standards for pain syndromes described in the literature, the discussion will be divided in four main topics, as these topics were treated during the SIMPAR (Study In Multidisciplinary PAin Research) meeting, held on December 2010 in Pavia: pathophysiology of pain, acute postoperative pain, opioids and pain, and chronic pain (Failed Back Surgery Syndrome). In the chapter of pathophysiology of pain we analyzed how to obtain a more personalized treatment through the study of the genetic and neurophysiological characteristics of patients and how to select the right local anesthetic according to anatomic and metabolizing patterns of patients. In acute postoperative pain we focalized our attention on the evidence supporting the use of continuous peripheral nerve blocks in the treatment of postoperative pain and in the prevention of chronic persistent post-operative pain, with a special attention in preventing side effects of regional anesthesia. We also reviewed the current evidence about the use of new very interesting modality to control postoperative pain after laparoscopy: pre-emptive nebulization of local anesthetic in abdominal cavity. As opioids are currently widely used to control chronic oncologic and non-oncologic pain, in this review we analyzed the level of evidence for their use, how to manage them better and psychological factors that can affect their success and/or determine addiction. Finally, we summarized the current evidence about Failed Back Surgery Syndrome focalizing our attention both in diagnosing it correctly and treating this syndrome with specific knowledge of the anatomic space that we have to approach and applying the possible treatments depending on pain pathophysiology and patient characteristics. In conclusion, it is important to try to personalize even better the therapy of patients with acute and chronic pain through a more accurate knowledge of anatomy, pathophysiology of pain, pharmacokinetic of pain drugs and of new device/therapies available.

Incidence and impact of pain conditions and comorbid illnesses.

Davis JA, Robinson RL, Le TK, Xie J

J Pain Res. 2011;4:331-45. Epub 2011 Oct 10.

BACKGROUND: Individuals with pain often present with more than one painful condition. The purpose of this study was to characterize the rates of comorbidity, pain medication use, and health care costs for 23 selected pain conditions in a large health plan using administrative claims data from 2005 to 2007. **METHODS:** Eligible patients included 1,211,483 adults with at least one pain condition during the one-year study period. Pain condition cohorts were classified based on the first diagnosis present in the claims during the study period. **RESULTS:** Musculoskeletal pain conditions were among the most prevalent cohorts including low back pain, osteoarthritis, and fibromyalgia. Cancer pain was the least prevalent cohort. Conditions with the lowest illness severity included migraine and painful bladder syndrome cohorts, while cohorts with diabetic neuropathy, human immunodeficiency virus (HIV)-associated pain, and cancer pain were the most severe. Across cohorts, the mean number of comorbid pain conditions ranged from 1.39 (for cancer pain and migraine) to 2.65 (for multiple sclerosis/pain). High rates of mental health conditions were found in cohorts with

HIV-associated pain and multiple sclerosis pain (42.59% and 34.78%) and were lowest among cohorts with rheumatoid arthritis and psoriatic arthropathy (12.73% and 13.31%), respectively. Rates of sleep disorders ranged from 5.47% (for painful bladder syndrome) to 11.59% (for multiple sclerosis pain). Overall, patients averaged 3.53 unique pain medications during the study period. Considerable annual total health care costs were observed in the cancer pain cohort and the lowest costs were observed in the postherpetic neuropathy, surgically-induced pain, migraine, and irritable bowel syndrome cohorts. Costs attributed to pain were highest among the multiple sclerosis, HIV, and cancer pain cohorts. The highest pharmaceutical costs were observed in the HIV cohort. **CONCLUSION:** These findings underscore the heterogeneity of patients with pain in terms of burden of illness, costs to the health care system, and the complexity of commonly co-occurring disorders.

Sex and pain perception and analgesia.

Palmeira CC, Ashmawi HA, Posso Ide P
Rev Bras Anesthesiol. 2011 Nov;61(6):814-28.

Sex is an important factor in painful experience modulation. Large volume of evidence shows that experience is different for males and females, as well as the answer to some classes of analgesics. Laboratory experiments suggest that women have a lower pain threshold than men related to pain from noxious stimuli such as heat, cold, pressure and electrical stimulation. Pain is a dynamic phenomenon under the influence of various mechanisms of excitatory and inhibitory control. The differences in pain perception related to sex may be associated with hyperalgesia in women, but also to the hypoactivity of the inhibitory system of pain in females. The purpose of this review besides showing some relationship for gonadal hormones, central nervous system and pain is to provide reference points for the discussion of one of the most intriguing aspects of the pathophysiology of pain: the differences in the presence of painful stimuli related to gender.

Current states of opinion and future directions on the epidemiology of sex differences in human pain.

Vigil JM
Pain Res Manag. 2011 Sep-Oct;16(5):317-9.

One of the most commonly neglected findings in the human pain literature is the observation of sex differences in the mechanisms that support the phenotypic expression of pain. The present commentary describes an assessment of the prevalence of observed sex differences in various pain processes, and of how expert pain researchers interpret the epidemiology and, hence, the proximate and ultimate causes of such differences. Forty-two pain investigators completed an anonymous survey on the epidemiology of sex differences in the human pain experience. Investigator responses indicated that sex differences are pervasive across various areas of pain research, that sex differences are particularly pronounced in the area of situational influences on pain behaviors, and that contemporary pain researchers

largely disagree on the epidemiology of, and hence, proximate and ultimate causes of the differences. The relevance of social situational factors on sex differences in pain behaviours is discussed in the context of evolutionary, developmental, social psychology and pain sensory systems that may function, in part, for regulating interpersonal intimacy.

Toll-like receptors in chronic pain.

Nicotra L, Loram LC, Watkins LR, Hutchinson MR
Exp Neurol. 2011 Oct 6. [Epub ahead of print]

Proinflammatory central immune signaling contributes significantly to the initiation and maintenance of heightened pain states. Recent discoveries have implicated the innate immune system, pattern recognition Toll-like receptors in triggering these proinflammatory central immune signaling events. These exciting developments have been complemented by the discovery of neuronal expression of Toll-like receptors, suggesting pain pathways can be activated directly by the detection of pathogen associated molecular patterns or danger associated molecular patterns. This review will examine the evidence to date implicating Toll-like receptors and their associated signaling components in heightened pain states. In addition, insights into the impact Toll-like receptors have on priming central immune signaling systems for heightened pain states will be discussed. The influence possible sex differences in Toll-like receptor signaling have for female pain and the recognition of small molecule xenobiotics by Toll-like receptors will also be reviewed.

Vulvovaginal Disorders

Chronic vulvovaginitis in women older than 50 years: Analysis of a prospective database.

Nyirjesy P, Leigh RD, Mathew L, Lev-Sagie A, Culhane JF
J Low Genit Tract Dis. 2011 Sep 29. [Epub ahead of print]

OBJECTIVE.: This study aimed to examine differences in symptoms and diagnoses between women 50 years and younger and women older than 50 years who have chronic vulvovaginal complaints. **METHODS:** New patients of the Drexel University Vaginitis Center with chronic vulvovaginal complaints were eligible. Participants underwent a standardized medical evaluation and completed detailed questionnaires. Data were analyzed using the t test, χ test, and the Fisher exact test. **RESULTS.:** Subjects were 469 women aged 18 to 79 years. Subjects 50 years and younger (group A) were more likely to complain of vaginal itching and were less likely to complain of burning, irritation, or soreness ($p \leq .05$ for all). Subjects older than 50 years (group B) were more likely to be diagnosed with atrophic vaginitis ($p = .000$), desquamative inflammatory vaginitis (DIV; $p = .001$), lichen planus (LP; $p = .000$), and lichen sclerosus ($p = .000$). Diagnosis of LS, LP, or DIV was associated with increased likelihood of multiparity and decreased likelihood of a history of systemic estrogen use.

CONCLUSIONS: Postmenopausal women are more likely than premenopausal women to be diagnosed with DIV, LP, or LS. Both childbirth and estrogen nonuse were associated with the occurrence of these latter 3 conditions.

The effect of "breathable" panty liners on the female lower genital tract.

Giraldo PC, Amaral RL, Juliato C, Eleutério J Jr, Brolazo E, Gonçalves AK
Int J Gynaecol Obstet. 2011 Oct;115(1):61-4. Epub 2011 Jul 27.

OBJECTIVE: To evaluate whether the use of "breathable" panty liners (BPLs) alters the normal vaginal flora, increases the incidence of bacterial vaginosis and/or vaginal candidiasis, or causes vulvar irritation. **METHODS:** A randomized controlled trial assessed the vaginal ecosystem of women without complaints of vaginal discharge. The study group (n=53) wore BPLs for 10-12 hours each day for 75 consecutive days, whereas the control group (n=54) wore only their usual underwear. At each of 6 visits during 3 menstrual cycles, participants underwent gynecologic examination with colposcopic evaluation and pH measurement, in addition to assessment of vaginal microbial flora, intensity of inflammatory processes, and presence of vaginal candidiasis/bacterial vaginosis in Gram-stained smears.

RESULTS: After 75 consecutive days of BPL use, 40/44 (90.9%) and 42/44 (95.5%) women reported no complaints of vaginal discharge or vulvar itching/burning, respectively. There was no significant difference between the study group and the control group with regard to positive vaginal fungus cultures (5/44 [11.4%] vs 8/50 [16.0%]; P=0.7848) or bacterial vaginosis (3/44 [6.8%] vs 2/50 [4.0%]; P=0.7974) at the end of the study period. **CONCLUSION:** After 75 days of BPL use, there was no significant increase in vulvovaginal candidiasis, bacterial vaginosis, vulvovaginal irritation, or vulvovaginal inflammation.

What causes chronic idiopathic perineal pain?

Hompes R, Jones OM, Cunningham C, Lindsey I
Colorectal Dis. 2011 Sep;13(9):1035-9. doi: 10.1111/j.1463-1318.2010.02422.x.

AIM: Chronic idiopathic perineal pain is poorly understood. Underlying structural abnormalities have been clinically suspected but rarely demonstrated objectively. The condition has been frequently considered to be a psychological disorder. We aimed to evaluate how commonly a structural explanation for such pain symptoms is present. **METHOD:** Patients seen in a pelvic floor clinic with severe chronic functional anorectal pain that was classified as chronic idiopathic perineal pain (study group) were prospectively registered in a pelvic floor database and underwent pelvic floor work up (defaecating proctography, anorectal physiology and anal ultrasound +/- rectal examination under anaesthetic). A control group was formed by patients with obstructed defaecation, with or without faecal incontinence, with advanced posterior compartment prolapse. **RESULTS:** Of 59 patients with chronic idiopathic perineal pain [80% women; mean age 53 (range, 22-84) years], representing 5% of all pelvic floor presentations, 33 (56%) had chronic idiopathic perineal pain alone and 26 (44%) had chronic idiopathic perineal pain with obstructed defaecation. Thirty-five (59%) had an underlying high-

grade internal rectal prolapse (73% with chronic idiopathic perineal pain + obstructed defaecation vs 48% with chronic idiopathic perineal pain alone; $P < 0.05$). Anorectal pain was present in 50% of 543 controls with advanced posterior compartment prolapse. **CONCLUSION:** High-grade internal rectal prolapse commonly underlies chronic idiopathic perineal pain, particularly when obstructed defaecation is present. Chronic anorectal pain is a common, under-recognized subsidiary symptom in patients with advanced posterior compartment prolapse presenting primarily with obstructed defaecation or faecal incontinence.

Risk factors for exposure, pain, and dyspareunia after tension-free vaginal mesh procedure.

Withagen MI, Vierhout ME, Hendriks JC, Kluivers KB, Milani AL
Obstet Gynecol. 2011 Sep;118(3):629-36.

OBJECTIVE: To identify possible risk factors for exposure, dyspareunia, and pain after insertion of tension-free vaginal mesh in pelvic organ prolapse surgery. **METHODS:** This was a prospective observational cohort study. Consecutive women who underwent surgery with a trocar-guided tension-free vaginal mesh kit were included and evaluated at 6 weeks and at 6 and 12 months after surgery with respect to anatomy and complications. Logistic regression analysis was performed to identify risk factors for exposure, dyspareunia, and pain. **RESULTS:** Two hundred ninety-four patients were included. Exposure was found in 34 patients (12%). Smoking and total mesh were risk factors for exposure (odds ratio [OR] 3.1, 95% confidence interval [CI] 1.1-8.7 and OR 3.0, 95% CI 1.2-7.0, respectively). Clinical and surgical experience were inversely related to the risk of exposure (OR 0.5, 95% CI 0.3-0.8 per decade). Pain (OR 3.2, 95% CI 1.2-8.4) and dyspareunia (OR 4.7, 95% CI 1.7-12.8) before surgery were predictive for pain and dyspareunia after surgery, respectively. Pain after surgery was found in 35 out of 275 (13%) patients and dyspareunia was found in 77 out of 171 (45%) patients. **LEVEL OF EVIDENCE:** Smoking, total tension-free vaginal mesh, and experience were predictive factors for mesh exposure.

Complications of polypropylene mesh for the treatment of female pelvic floor disorders.

García SL, Ramírez DL, Rey JR, Calvo JF, Iglesias BR, Calvo AO
Arch Esp Urol. 2011 Sep;64(7):620-8.

OBJECTIVES: To assess the complications of polypropylene mesh in the treatment of female pelvic floor disorders. **METHODS:** retrospective study of patients with pelvic floor pathology (SUI, cystocele, rectocele, enterocele) undergoing pelvic floor intervention with surgical meshes from March 2002 to October 2009. We evaluated complications, effectiveness of the technique and distribution of the impact of the results. For statistical analysis SPSS software was used and the curve of impact was estimated by Cox model. **RESULTS:** We analyzed 363 patients. Of these 363 patients, 290 (79.9%) suffered from Stress Urinary Incontinence 37 (10.2%)cystocele, 33 (9.4%) SUI and cystocele, 1 (0.3%) SUI and enterocele, 1 (0.3%) cystocele and enterocele and 1 (0.3%) cystocele, enterocele and rectocele. The interventions done were: 34 (9.4%) anterior and middle compartment meshes, 1 (0.3%) middle and posterior compartment meshes, 1

(0.3%) TOT and middle and posterior compartment mesh, 36 (9.9%) TVT and 3 (0.8%) TVT and anterior and middle compartment mesh. The median follow-up was 36 (3-90) months. 50 patients (13.8%) presented complications: 21 (42%) had lower urinary tract irritative symptoms, 10 (20%) externalization of the mesh, 3 (6%) necrotizing fasciitis, 3 (6%) obturator fossa, thigh root or vaginal abscess, 5 (10%) chronic pelvic pain, thigh pain or dyspareunia, 2 (4%) bruising and bleeding, 3 (6%) urinary tract infections, 1 (2%) mesh entering bladder and 2 (4%) obstructive symptoms. The procedures were effective in 350 (96.4%) patients. The impact of complications was manifested in the first 10 months after surgery. **CONCLUSIONS:** Polypropylene meshes are very effective in the treatment of female pelvic floor disorders. Approximately 10% of the patients had complications that resolved spontaneously or with medical treatment in most cases. One third of the complications are subsidiaries of surgery, by removing the mesh totally or partially, without affecting the intervention results.

Common vulval dermatoses.

Drummond C

Aust Fam Physician. 2011 Jul;40(7):490-6.

BACKGROUND: The vulva is skin, and it is helpful to approach vulval conditions from a dermatological perspective. The vulva is affected by the same dermatoses as the rest of the skin, but modified in appearance by special influences. **OBJECTIVE:** This article will outline an approach to the diagnosis and management of vulval dermatoses. **DISCUSSION:** Vulval disorders present as infections, rashes and lesions, and pain. This article considers inflammatory vulval disorders that present as erythematous rashes, pallor or erosions and ulcers. Most vulval dermatoses are recurrent or chronic and may require maintenance therapy. Chronic painful and itchy vulval conditions can lead to secondary pelvic floor spasm and a sensory neuropathy. Many vulval disorders are multifactorial and can benefit from a multidisciplinary approach to management.

Dermaisilk briefs in vulvar lichen sclerosus: an adjuvant tool.

D'Antuono A, Bellavista S, Negosanti F, Zauli S, Baldi E, Patrizi A

J Low Genit Tract Dis. 2011 Oct;15(4):287-91. doi: 10.1097/LGT.0b013e31821380a0.

OBJECTIVE: The purpose of our study was to evaluate whether briefs made of Dermaisilk fabric could be an adjuvant tool in the management of vulvar lichen sclerosus (LS). **MATERIALS AND METHODS:** A controlled, randomized, double-blind study versus placebo was conducted, comparing Dermaisilk versus standard cotton briefs in patients affected by LS during treatment with clobetasol propionate 0.05% ointment and vitamin E moisturizer. For each patient, an evaluation of objective genital signs and subjective symptoms typical of LS was recorded before the start of treatment, after 1 month, and after 6 months of the study. Statistical analysis was performed with SPSS 17.0 for Windows. **RESULTS:** Forty-two women affected by LS were recruited and divided into those wearing Dermaisilk or cotton briefs. Patients wearing Dermaisilk briefs showed a better improvement in the clinical symptoms of burning sensation, skin

irritation, and pain (Fisher test, $p < .0001$) compared with the cotton placebo group. The improvement in itching was also faster in the Dermasilk group (Fisher exact test, $p < .05$). Erythema also showed a better improvement in the Dermasilk group (Fisher test, $p < 0.05$).
CONCLUSIONS: Dermasilk fabric seems to be a useful adjunct to topical treatment in producing a better and more rapid control of symptoms in patients with LS.

Lichen sclerosus and squamous cell carcinoma.

Gutiérrez-Pascual M, Vicente-Martín FJ, López-Esteban JL
Actas Dermosifiliogr. 2011 Nov 9. [Epub ahead of print]

Lichen sclerosus is a chronic inflammatory disease that can progress to malignancy. The literature indicates an association with anogenital squamous cell carcinoma and verrucous carcinoma. Two pathogenic pathways, differentiated vulvar and penile intraepithelial neoplasias, which have recently been described in relation to squamous cell carcinoma, are both highly associated with genital lichen sclerosus independently of human papilloma virus (HPV) infection. Furthermore, tumor-promoting molecular changes unrelated to HPV infection have been demonstrated and may explain the malignant potential of lichen sclerosus. The possible relationship between HPV and genital lichen sclerosus currently remains open to discussion, and the prognostic importance of the overlapping of these 2 diseases is still unclear. This review considers the relationship between lichen sclerosus and squamous cell and verrucous carcinomas, the possible oncogenic mechanisms involved, and their possible association with HPV infection.

Topical tacrolimus ointment for the treatment of lichen sclerosus, comparing genital and extragenital involvement.

Kim GW, Park HJ, Kim HS, Kim SH, Ko HC, Kim BS, Kim MB
J Dermatol. 2011 Nov 2. doi: 10.1111/j.1346-8138.2011.01384.x. [Epub ahead of print]

Lichen sclerosus is a chronic inflammatory dermatosis presenting with significant sclerosis, atrophy and pruritus. The treatment for this condition remains unsatisfactory, with potent corticosteroids being the most effective therapy. In this study, we investigated the efficacy and safety of tacrolimus ointment in patients with genital and extragenital lichen sclerosus. Sixteen patients with active lichen sclerosus (10 with anogenital and six with extragenital localization) were treated with topical tacrolimus ointment twice daily. The therapeutic effects were evaluated according to 3 grades: complete response (>75% improvement), partial response (25-75% improvement), or no response (<25% improvement). Applications were continued until complete disappearance or stabilization of the cutaneous lesions. In addition, we conducted telephone surveys to determine the long-term treatment outcome and relapse rate. Objective response to therapy occurred in nine of 10 patients (90%) with anogenital and one of six patients (16.7%) with extragenital lesions. Out of 10 patients with anogenital lichen sclerosus, five showed more than 75% improvement. Complete, partial and no response were achieved in five (50%), four (40%) and one (10%) patient, respectively. During the follow-up period of a

mean of 29.3 months, six of nine patients had a relapse of symptoms. However, most patients with extragenital involvement did not respond to tacrolimus, except one patient showing partial response. No significant adverse effects were observed. Topical tacrolimus ointment was a safe and effective treatment for genital lichen sclerosus and should be used for long-term duration to prevent relapse. However, it was not useful for patients with extragenital lichen sclerosus.

Topical TRPM8 Agonist (Icilin) relieved vulva and pruritus originating from lichen sclerosus et atrophicus.

Han JH, Choi HK, Kim SJ

Acta Derm Venereol. 2011 Nov 1. doi: 10.2340/00015555-1244. [Epub ahead of print]

No abstract available.

High frequency of genital lichen sclerosus in a prospective series of 76 patients with morphea: Toward a better understanding of the spectrum of morphea.

Lutz V, Francès C, Bessis D, Cosnes A, Kluger N, Godet J, Sauleau E, Lipsker D

Arch Dermatol. 2011 Oct 17. [Epub ahead of print]

OBJECTIVE: To compare the frequency of genital lichen sclerosus (LS) in patients with morphea with that of control patients. **DESIGN:** A prospective multicenter study. **SETTING:** Four French academic dermatology departments: Strasbourg, Montpellier, Tenon Hospital Paris, and Henri Mondor Hospital Créteil. **Patients** Patients were recruited from November 1, 2008, through June 30, 2010. Seventy-six patients with morphea and 101 age- and sex-matched controls, who underwent complete clinical examination, were enrolled. **Interventions:** A complete clinical examination and, if deemed necessary, a cutaneous biopsy. **Main Outcome Measure:** The frequency of genital LS. **RESULTS:** There were 58 women and 18 men (a 3:1 ratio) with a median age of 59 years. Mean (range) age at diagnosis was 54 (13-87) years. Forty-nine patients had plaque morphea, 9 had generalized morphea, and 18 had linear morphea. Three patients (3%) in the control group and 29 patients (38%) with morphea had LS (odds ratio, 19.8; 95% CI, 5.7-106.9; $P < .001$). Twenty-two patients with plaque morphea (45%) and only 1 patient with linear morphea (6%) had associated genital LS. **CONCLUSIONS:** Genital LS is significantly more frequent in patients with morphea than in unaffected individuals. Forty-five percent of patients with plaque morphea have associated LS. Complete clinical examination, including careful inspection of genital mucosa, should therefore be mandatory in patients with morphea because genital LS bears a risk of evolution into squamous cell carcinoma and thus needs treatment with topical corticosteroids.

Health-related quality of life and patient-defined benefit of clobetasol 0.05% in women with chronic lichen sclerosis of the vulva.

Schwegler J, Schwarz J, Eulenburg C, Blome C, Ihnen M, Mahner S, Jaenicke F, Augustin M, Woelber L
Dermatology. 2011 Oct 11. [Epub ahead of print]

BACKGROUND: This study investigates the health-related quality of life in patients with vulvar lichen sclerosis (LS) and the patient-defined therapeutic benefit of clobetasol. **Methods:** A survey analysis of 96 women with LS after treatment with clobetasol was performed. Quality of life was assessed with the Skindex-29. The Patient Benefit Index (PBI) was used to determine the therapeutic benefit. **RESULTS:** The overall response rate was 59.2%. Quality of life was most impaired by somatic symptoms (scale 'Symptoms' score 3.2) and emotional stress (scale 'Emotions' score 3.1), while social interactions (scale 'Functioning' score 1.9) played an inferior role ($p < 0.001$). Primary therapeutic goals 'to have confidence in the therapy' and 'to be free of itching' were achieved in 73.2 and 69.0% of patients who indicated the goal applied to them. The global PBI score was 3.06. In 93.2% of patients it was >1 , indicating a potential benefit from clobetasol. **CONCLUSION:** Topical clobetasol is of potential therapeutic benefit for patients with vulvar LS and might therefore improve quality of life.

Pyosalpinx as a sequela of labial fusion in a post-menopausal woman: a case report.

Tsianos GI, Papatheodorou SI, Michos GM, Koliopoulos G, Stefos T
J Med Case Reports. 2011 Nov 6;5(1):546. [Epub ahead of print]

INTRODUCTION: Complete labial fusion is a rare clinical entity in post-menopausal women. The most common complications of this presentation are infections of the urinary tract and retention of urine in the vagina. We present the case of a post-menopausal woman with adnexal mass and abdominal pain due to fusion of the labia majora. To the best of our knowledge this is the first report in the literature of this complication. **CASE PRESENTATION:** A 78-year-old Caucasian woman was admitted to our hospital due to abdominal pain and urination difficulty, along with fever and leucocytosis. On examination the labial majora were fused. Computed tomography of the abdomen revealed a cystic formation in the anatomical area of the right adnexa. Our patient had developed a pyosalpinx as a Sequela of labial fusion. At laparoscopy the right pyosalpinx was identified and resected, whereas the labia majora were reconstructed via dissection and separation. **CONCLUSIONS:** Labial fusion is a rare clinical entity in post-menopausal women and can have serious and unexpected complications. Though this presentation is rare, a clinical examination must be performed in detail in order to gain valuable information for an accurate diagnosis. Post-operational instruction must be given to patients in order to prevent the re-occurrence of the fusion and its complications.

The role of examination under anesthesia (EUA) and vaginoscopy in pediatric and adolescent gynecology: a retrospective review.

Nakhal RS, Wood D, Creighton SM

J Pediatr Adolesc Gynecol. 2011 Nov 1. [Epub ahead of print]

BACKGROUND: Examination under anesthesia (EUA) with diagnostic vaginoscopy is an invaluable method in the lower genital tract assessment of pediatric and adolescent females. The literature on this topic remains scarce. **METHODS:** This is a retrospective medical notes review of all patients who underwent EUA with or without vaginoscopy over the past 5 years at a pediatric and adolescent gynecology unit specializing in disorders of sex development (DSD). **RESULTS:** From 2005 to 2010, 83 patients underwent 92 procedures. All procedures were performed under general anesthesia, and a 3-mm pediatric cystoscope was used for vaginoscopy. Of the 92 cases, 33 (36%) were EUA alone and 59 (64%) consisted of a combined EUA and vaginoscopy. The mean age was 13.3 ± 3.7 years. The most common indications included assessment for reconstructive surgery (33.7%), vaginal stenosis (21.7%), vaginal discharge (19.6%), vaginal bleeding (16.3%), and pelvic pain (8.7%). Most (61%) of those presenting for assessment for reconstructive surgery had a DSD and history of surgical correction in early childhood. In 88 cases (96%), the evaluation was satisfactory and a diagnosis was reached or normality confirmed. Four cases (4%) required further investigation. No significant intraoperative or postoperative complications were encountered. Of the 92 cases, 15 (16%) required a further minor procedure, which was performed at the time of the EUA/vaginoscopy. Another 33 (36%) required further major surgery, which was performed at a later date. **CONCLUSION:** EUA/vaginoscopy is a safe and highly useful method in the assessment of the lower genital tract in pediatric and adolescent patients.

Interventions for prevention and treatment of vulvovaginal candidiasis in women with HIV infection.

Ray A, Ray S, George AT, Swaminathan N

Cochrane Database Syst Rev. 2011 Aug 10;(8):CD008739.

BACKGROUND: Vulvovaginal candidiasis (VVC) is one of the most common fungal infections that recur frequently in HIV infected women. Symptoms of VVC are pruritis, discomfort, dyspareunia, and dysuria. Vulval infection presents as a morbiliform rash that may extend to the thighs. Vaginal infection is associated with white discharge, and plaques are seen on erythematous vaginal walls. Even though rarely or never resulting in systemic fungal infection or mortality, left untreated these lesions contribute considerably to the morbidity associated with HIV infection. Prevention and treatment of this condition is an essential part of maintaining the quality of life for these individuals. **OBJECTIVES:** To compare the efficacy of various antifungals given vaginally or orally for the treatment and prophylaxis of VVC in HIV-infected women and to evaluate the risks of the same. **SEARCH STRATEGY:** The search strategy was comprehensive, iterative and based on that of the HIV/AIDS Cochrane Review Group. The aim was to locate all relevant trials, irrespective of publication status or language. Electronic databases: CENTRAL, Medline, EMBASE, LILACS and CINAHL were searched for randomised controlled trials for the

years 1980 to 1st October 2010. WHO ICTRP site and other relevant web sites were also searched for conference abstracts. SELECTION CRITERIA: Randomised controlled trials (RCTs) of palliative, preventative or curative therapy were considered. Participants were HIV positive women receiving one or more of the following: treatment / prophylaxis for VVC or HAART (Highly Active Antiretroviral Therapy). DATA COLLECTION AND ANALYSIS: Three authors independently assessed the methodological quality of the trials and extracted data. The quality of the evidence generated was graded using the GRADE PRO approach. MAIN RESULTS: Our search did not yield any trial investigating treatment of VVC in HIV positive women. Two trials dealing with prophylaxis were eligible for inclusion. One trial (n= 323) favoured the use of weekly Fluconazole as compared to placebo (RR 0.68; 95% CI 0.47 to 0.97). The second trial with three arms of comparison; Clotrimazole, Lactobacillus and Placebo gave no definitive results in preventing an episode of VVC. Clotrimazole against placebo (RR 0.49; 95% CI 0.22 to 1.09), Clotrimazole against lactobacillus (RR 1.11; 95% CI 0.45 to 2.76) and lactobacillus against placebo (RR 0.54; 95% CI 0.26 to 1.13). AUTHORS' CONCLUSIONS: Implications for practice: No trials were found addressing treatment of VVC in HIV positive women. In comparison to placebo, Fluconazole was found to be an effective preventative intervention. However, the potential for resistant *Candida* organisms to develop might impact the feasibility of implementation. Direction of findings suggests that Clotrimazole and Lactobacillus improved the prophylactic outcomes when compared to placebo. Implications for research: There is a need to evaluate drugs and drug regimens for VVC treatment and prophylaxis in HIV positive women through randomised clinical trials. Development of resistance to azoles remains under-studied and more work must be done in this area, so as to determine whether routine prophylaxis for VVC is at all needed or whether adequate ART would be sufficient to prevent recurrent VVC. The viral load in vaginal secretions with or without treatment or prophylaxis has not been studied, this is very relevant to the spread of HIV.

Distribution of *Candida albican* genotype and *Candida* species is associated with the severity of vulvovaginal candidiasis.

Zeng J, Zong LL, Mao T, Huang YX, Xu ZM

Nan Fang Yi Ke Da Xue Xue Bao. 2011 Oct;31(10):1649-53.

OBJECTIVE: To investigate the distribution of pathogenic *C. albican* genotype and *Candida* species in association with the severity of vulvovaginal candidiasis (VVC).

METHODS: Polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) of the internal transcribed spacer analysis was employed to identify the *Candida* species isolated from the vaginal secretions of 198 patients with acute VVC. SSCP and GeneScan analyses of microsatellite locus I polymorphism were used to determine the genotypes of the clinical isolates of *C. albican* associated with VVC. All the patients were scored for clinical signs and symptoms to evaluate the severity of VVC. RESULTS: A total of 198 *Candida* strains were isolated from VVC patients, including 140 (70.7%) *C. albicans* strains and 58 (29.3%) non-*albicans* strains. In the 95 patients with severe VVC and 103 with mild-moderate VVC, *C. albican* was detected in 62.1% and 76.6% of the patients, respectively (P=0.011). Thirty-eight microsatellite locus I genotypes were detected in 140 unrelated *C. albican* strains, among which

the dominant genotypes 30-45 (44 strains, 31.43%) and 32-46 (23 strains, 16.43%) were the most common, followed by genotypes 30-46 (4 strains, 2.86%) and 32-47 (9 strains, 6.42%). The overall frequencies of the 4 genotypes were significantly higher in severe VVC than in mild-moderate VVC cases (77.9% vs 42.0%, $P < 0.001$). **CONCLUSION:** *C. albicans* remains the most common pathogenic *Candida* species in patients with VVC, but the non-*albicans* species seem more likely to cause severe VVC. The dominant genotypes of *C. albicans* with a tropism for the vagina are correlated to the severity of VVC.

Insights from human studies into the host defense against candidiasis.

Filler SG

Cytokine. 2011 Oct 17. [Epub ahead of print]

Candida spp. are the most common cause of mucosal and disseminated fungal infections in humans. Studies using mutant strains of mice have provided initial information about the roles of dectin-1, CARD9, and Th17 cytokines in the host defense against candidiasis. Recent technological advances have resulted in the identification of mutations in specific genes that predispose humans to develop candidal infection. The analysis of individuals with these mutations demonstrates that dectin-1 is critical for the host defense against vulvovaginal candidiasis and candidal colonization of the gastrointestinal tract. They also indicate that CARD9 is important for preventing both mucosal and disseminated candidiasis, whereas the Th17 response is necessary for the defense against mucocutaneous candidiasis. This article reviews the recent studies of genetic defects in humans that result in an increased susceptibility to candidiasis and discusses how these studies provide new insight into the host defense against different types of candidal infections.

Assessment of in vitro biofilm formation by Candida species isolates from vulvovaginal candidiasis and ultrastructural characteristics.

Paiva LC, Vidigal PG, Donatti L, Svidzinski TI, Consolaro ME

Micron. 2011 Sep 29. [Epub ahead of print]

Vulvovaginal candidiasis (VVC) is a very common cause of fungal infection that remains a significant problem worldwide, especially concerning its complex pathogenicity. Biofilm dynamics from vaginal isolates requires further investigation. Different assays, such as cell surface hydrophobicity (CSH), biofilm production, fungal metabolism by 2H-tetrazolium-5-carboxanilide (XTT) and phenazine methosulfate (PMS), scanning electron microscopy (SEM) and confocal scanning laser microscopy (CSLM) were used in order to determine the ability of five *Candida* species isolates from VVC patients to form in vitro biofilms and their ultrastructural characteristics. All yeasts demonstrated the ability to produce biofilm and showed viability up to 48h after the completion of assay, confirmed by SEM and CSLM, but differences were observed between them. SEM and CSLM also revealed that all VVC isolates adhered only in blastoconidia form, except for *Candida parapsilosis*. Even though, only one isolate from each *Candida* species has been used, the results of high biofilm formation, metabolic activity and

CSH showed by *Candida albicans* and *C. parapsilosis*, as well as by the ultrastructural characteristics, suggest that these species exhibit greater ability of adherence in relation to the others. Ours results support the theory that virulence potential is multifactorial and that other factors not evaluated in this study could be involved in the CVV physiopathogeny.

Oral fluconazole 150mg single dose versus intra-vaginal clotrimazole treatment of acute vulvovaginal candidiasis.

Sekhavat L, Tabatabaai A, Tezerjani FZ
J Infect Public Health. 2011 Sep;4(4):195-9.

OBJECTIVE: To compare the safety and efficacy of fluconazole 150mg single dose and intra-vaginal clotrimazole 200mg per day for six days in the treatment of the acute episode of vulvovaginal candidiasis (VVC). **METHODS:** In a prospective study, 142 patients with acute clinical and mycological confirmed VVC were enrolled and divided randomly in two groups. 70 patients received intra-vaginal tablet (200mg) daily for seven days, whereas 72 patients received single dose oral fluconazole (150mg). Second and third visits were done for all patients seven days and one month after treatment and the clinical and mycological outcomes evaluated. The analysis performed using SPSS statistical software (version 15). **RESULTS:** At the second visit, 61 patients (84.7%) were cured clinically (inflammation and discharge) and 58 patients (80.5%) mycologically in fluconazole group and 60 patients (83.3%) were cured clinically and 49 patients (70%) mycologically in clotrimazole group ($P=0.01$). At the third visit, only one patient in fluconazole group and 17 patients in clotrimazole group had clinical sign of VVC ($P=0.001$). **CONCLUSION:** Oral fluconazole single dose seems to be a valid and promising therapy to cure acute signs and symptoms of VVC.

Vulvovaginal candidiasis in postmenopausal women: the role of hormone replacement therapy.

Fischer G, Bradford J
J Low Genit Tract Dis. 2011 Oct;15(4):263-7. doi: 10.1097/LGT.0b013e3182241f1a.

OBJECTIVE: This study aimed to explore the role of hormone replacement therapy (HRT) in susceptibility to vulvovaginal candidiasis (VVC) in a private vulval disease referral practice. **METHODS:** Between January 2009 and December 2010, 149 healthy, nondiabetic patients with vulvar conditions were compared for significant differences in vaginal swab result, age, and diagnosis between those using and not using HRT. Detailed clinical data were collected from those with VVC. **RESULTS:** The mean ages of the HRT ($n = 70$) and non-HRT ($n = 79$) groups were 62.5 and 62.5 years, respectively. Positive cultures for *Candida* were found in 34 (48.5%) of 70 patients on HRT and in 2 (3%) of 79 subjects not on HRT ($p < .001$). Culture-positive, clinical VVC was identified in 34 (49%) of 70 patients on HRT and in 1 (1%) of 79 patients not on HRT ($p < .001$). *Candida* species (32 *Candida albicans* and 2 *Candida glabrata*) were isolated from the 34 VVC patients, and of these, 23 (67%) had a history of recurrent or chronic candidiasis before menopause. All 34 had been previously treated with antifungal

therapy without ceasing HRT and had been unresponsive to treatment or had relapse after treatment. In 27 (79%) of 34 patients, HRT was suspended during treatment. Of those who remained on HRT during treatment or resumed it after treatment, prophylactic antifungal treatment was initiated in 15 (44%) to prevent recurrence. All patients responded to the antifungal treatment provided HRT was suspended or prophylactic treatment was used. CONCLUSIONS: Postmenopausal women taking HRT are significantly more prone to develop VVC than women who are not and those with VVC are likely to have been susceptible to it before menopause.

Efficacy of fluconazole and nystatin in the treatment of vaginal *Candida* species.

Martins HP, da Silva MC, Cássia L, Svidzinski TI, Consolaro ME

Acta Derm Venereol. 2011 Sep 15. doi: 10.2340/00015555-1194. [Epub ahead of print]

The aim of this study was to determine and compare the efficacy of treatment with fluconazole and nystatin in Brazilian women with vaginal *Candida*. In a population of 932 women, vaginal cultures were performed for yeasts, whether or not the women showed signs and symptoms of vulvovaginal candidiasis. Yeasts were isolated from 12.2% of the women (114/932): 53.2% of the yeasts were *Candida albicans*, 27.0% *C. glabrata*, 13.5% *C. tropicalis* and 6.3% *C. parapsilosis*. Treatment was carried out with both drugs. The overall mean cure rates with fluconazole (87.0%) and nystatin (74.0%) were similar; among women with non-*albicans*, the cure rate with fluconazole was 100%, whereas that with nystatin was 44.4%. The cure rate for women with *C. albicans* was high with both fluconazole and nystatin; however, for those with non-*albicans* species the cure rate was excellent with fluconazole and very low with nystatin, differing from the majority of in vitro studies.

A screening assay based on host-pathogen interaction models identifies a set of novel antifungal benzimidazole derivatives.

Burger-Kentischer A, Finkelmeier D, Keller P, Bauer J, Eickhoff H, Kleymann G, Abu Rayyan W, Singh A, Schröppel K, Lemuth K, Wiesmüller KH, Rupp S

Antimicrob Agents Chemother. 2011 Oct;55(10):4789-801.

Fungal infections are a serious health problem in clinics, especially in the immune-compromised patient. Disease ranges from widespread superficial infections like vulvovaginal infections to life-threatening systemic candidiasis. Especially for systemic mycoses, only a limited arsenal of antifungals is available. The most commonly used classes of antifungal compounds used include azoles, polyenes, and echinocandins. Due to emerging resistance to standard therapy, significant side effects, and high costs for several antifungals, there is a medical need for new antifungals in the clinic and general practice. In order to expand the arsenal of compounds with antifungal activities, we screened a compound library including more than 35,000 individual compounds derived from organic synthesis as well as combinatorial compound collections representing mixtures of compounds for antimycotic activity. In total, more than 100,000 compounds were screened using a new type of activity-selectivity assay, analyzing both the

antifungal activity and the compatibility with human cells at the same time. One promising hit, an (S)-2-aminoalkyl benzimidazole derivative, was developed among a series of lead compounds showing potent antifungal activity. (S)-2-(1-Aminoisobutyl)-1-(3-chlorobenzyl) benzimidazole showed the highest antifungal activity and the best compatibility with human cells in several cell culture models and against a number of clinical isolates of several species of pathogenic *Candida* yeasts. Transcriptional profiling indicates that the newly discovered compound is a potential inhibitor of the ergosterol pathway, in contrast to other benzimidazole derivatives, which target microtubules.

Impact of pH on the antifungal susceptibility of vaginal *Candida albicans*.

Liu W, Zhang X, Liu Z, Luo X

Int J Gynaecol Obstet. 2011 Sep;114(3):278-80. Epub 2011 Jun 21.

OBJECTIVE: To investigate the antifungal susceptibility at pH 7.0 and pH 4.0 of 5 antifungal agents against *Candida albicans* isolated from patients with vulvovaginal candidiasis. **METHODS:** Antifungal susceptibility testing at pH 7.0 and pH 4.0 was performed using the broth microdilution method (CLSI, document M27-A2). **RESULTS:** The minimal inhibitory concentrations (MICs) of miconazole, clotrimazole, fluconazole, and nystatin against *C. albicans* at pH 4.0 were significantly higher than those at pH 7.0 (0.25 vs 0.03 µg/mL, 0.50 vs 0.03 µg/mL, 0.50 vs 0.25 µg/mL, and 32 vs 2 µg/mL, respectively; $P < 0.001$), whereas the MIC of itraconazole at pH 4.0 was lower than that at pH 7.0 (0.030 vs 0.125 µg/mL; $P < 0.001$). The susceptibility rate of *C. albicans* to itraconazole at pH 4.0 was significantly higher than at pH 7.0 (95.0% vs 51.7%; $P < 0.001$). The susceptibility rate to itraconazole at pH 7.0 was significantly lower than the susceptibility rate to fluconazole (51.7% vs 100.0%; $P < 0.001$), whereas the susceptibility rates to the 2 drugs were similar at pH 4.0 (95.0% and 96.7%, respectively). **CONCLUSION:** Media at different pH values should be used for sensitivity tests according to the environment of *C. albicans*.

Role of TP53 mutations in vulvar carcinomas.

Choschzick M, Hantaredja W, Tennstedt P, Giesecking F, Wölber L, Simon R

Int J Gynecol Pathol. 2011 Sep;30(5):497-504.

Human papillomavirus (HPV)-independent development of vulvar carcinomas is common and the disruption of the TP53 pathway seems to play a key role in these tumors. Overexpression of TP53 in precursor lesions (differentiated VIN) and associated invasive carcinomas is regarded as an important diagnostic feature of this subtype of vulvar cancer. To determine the relationship of TP53 mutation status with clinicopathologic parameters, HPV status, and patient outcome, 18 squamous cell carcinomas of the vulva with TP53 overexpression along with 21 immunohistochemically TP53-negative tumors were analyzed. TP53 mutations were found in 17 (43.6%) of vulvar cancers, 18 (46.2%) tumors were HPV associated, and 8 (20.5%) carcinomas showed no relation to HPV infection or TP53 mutations. The presence of TP53 mutations was significantly linked to TP53 overexpression ($P = 0.002$) and negative HPV status ($P = 0.012$). The

specificity of TP53 protein overexpression for the occurrence of TP53 mutations was 68.2%, with a positive predictive value of 66.7%. The most frequent mutation types were C:G →T:A transitions (57.9%). This mutation pattern strongly indicates the important role of oxidative stress in vulvar carcinogenesis. There were no relationships between TP53 mutation status and tumor stage, grading, nodal status, depth of invasion, or patient prognosis. In summary, TP53 mutations play a crucial role in a substantial proportion of vulvar carcinomas and are probably associated to cellular oxidative stress in chronically degenerative diseases of the vulva, such as lichen sclerosus. These data support the potential utility of restoring TP53 function as a therapeutic alternative in vulvar cancer. Further studies are necessary to clarify the prognostic implications of TP53 mutations in vulvar carcinomas.

Expression of TWEAK in normal human skin, dermatitis and epidermal neoplasms: association with proliferation and differentiation of keratinocytes.

Peternel S, Manestar-Blažič T, Brajac I, Prpić-Massari L, Kaštelan M

J Cutan Pathol. 2011 Oct;38(10):780-9. doi: 10.1111/j.1600-0560.2011.01762.x. Epub 2011 Jul 29.

BACKGROUND: Tumor necrosis factor-like weak inducer of apoptosis (TWEAK) has been implicated in the pathogenesis of various inflammatory pathologies and cancer. We aimed to investigate its expression in normal human skin, inflammatory skin diseases and epidermal neoplasms. **METHODS:** Immunohistochemistry for TWEAK was performed in samples of healthy skin, plaque psoriasis, lichen planus, prurigo nodularis, discoid lupus erythematosus, lichen sclerosus, seborrheic keratosis, common warts, actinic keratosis, Bowen's disease, keratoacanthoma and basal and squamous cell carcinoma. Double immunofluorescence was used to investigate co-localization of TWEAK with cytokeratin-10 and proliferating cell nuclear antigen (PCNA). **RESULTS:** TWEAK was robustly expressed in the epidermis of healthy skin and decreased in inflammatory conditions, both in the context of epidermal hyperplasia and atrophy. Decreased TWEAK immunoreactivity was regularly observed in common warts, actinic keratosis and Bowen's disease, particularly in areas of marked proliferation as evidenced by PCNA-positive nuclei. In squamous cell carcinoma, expression of TWEAK ranged from strong to completely absent, and it mostly corresponded with the expression of cytokeratin-10. TWEAK was absent in keratoacanthoma and basal cell carcinoma. **CONCLUSIONS:** TWEAK is a constitutively expressed epidermal protein whose downregulation might be an early indicator of disturbed differentiation or pathologic proliferation of keratinocytes that accompany inflammatory and neoplastic skin diseases.

Genital warts and vulvar intraepithelial neoplasia: natural history and effects of treatment and human immunodeficiency virus infection.

Massad LS, Xie X, Darragh T, Minkoff H, Levine AM, Watts DH, Wright RL, D'Souza G, Colie C, Strickler HD; Women's Interagency HIV Study Collaborative Study Group
Obstet Gynecol. 2011 Oct;118(4):831-9.

OBJECTIVE: To describe the natural history of genital warts and vulvar intraepithelial neoplasia (VIN) in women with human immunodeficiency virus (HIV). **METHODS:** A cohort of 2,791 HIV-infected and 953 uninfected women followed for up to 13 years had genital examinations at 6-month intervals with biopsy for lesions suspicious for VIN. **RESULTS:** The prevalence of warts was 4.4% (5.3% for HIV-seropositive women and 1.9% for HIV-seronegative women, $P<.001$). The cumulative incidence of warts was 33% (95% confidence interval [CI] 30-36%) in HIV-seropositive and 9% (95% CI 6-12%) in HIV-seronegative women ($P<.001$). In multivariable analysis, lower CD4 lymphocyte count, younger age, and current smoking were strongly associated with risk for incident warts. Among 501 HIV-seropositive and 43 HIV-seronegative women, warts regressed in 410 (82%) seropositive and 41 (95%) seronegative women ($P=.02$), most in the first year after diagnosis. In multivariable analysis, regression was negatively associated with HIV status and lower CD4 count as well as older age. Incident VIN of any grade occurred more frequently among HIV-seropositive than HIV-seronegative women: 0.42 (0.33-0.53) compared with 0.07 (0.02-0.18) per 100 person-years ($P<.001$). Positivity for VIN 2 was found in 58 women (55 with and three without HIV, $P<.001$). Two women with HIV developed stage IB squamous cell vulvar cancers. **CONCLUSION:** Although genital warts and VIN are more common among HIV-seropositive than HIV-seronegative women, wart regression is common even in women with HIV, and cancers are infrequent.

Is differentiated vulval intraepithelial neoplasia the precursor lesion of human papillomavirus-negative vulval squamous cell carcinoma?

Kokka F, Singh N, Faruqi A, Gibbon K, Rosenthal AN
Int J Gynecol Cancer. 2011 Oct;21(7):1297-305.

Vulval squamous cell carcinoma appears to arise via 2 distinct pathways. A significant minority are associated with oncogenic human papillomavirus (HPV) infection and undifferentiated vulval intraepithelial neoplasia (VIN). However, the majority arises in the absence of HPV, on a background of chronic inflammation. Until recently, it was assumed that lichen sclerosus was the underlying inflammatory condition in the majority of HPV-negative cancers. This pathway of carcinogenesis has been less well studied than the HPV pathway. Emerging evidence implicates differentiated VIN (DVIN), rather than lichen sclerosus, as the most likely precursor lesion in HPV-negative vulval squamous cell carcinoma. Here we discuss the clinical and molecular evidence that implicates DVIN as a lesion with a high malignant potential. This lesion is probably underdiagnosed and may be undertreated. Better recognition of DVIN by gynecologists and pathologists may therefore offer an opportunity to prevent some vulval cancers.

Immunohistochemical expression of survivin and γ -H2AX in vulvar intraepithelial neoplasia and low-stage squamous cell carcinoma.

Brustmann H, Hinterholzer S, Brunner A
Int J Gynecol Pathol. 2011 Nov;30(6):583-90.

Survivin inhibits apoptosis and is involved in the regulation of cell cycle progression and in the mitotic spindle formation. It is overexpressed in many cancers. The histone γ -H2AX is a marker of activated DNA damage and is overexpressed in different cancers and their precursor lesions. It also forms early during apoptosis. Eighty-seven formalin-fixed, paraffin-embedded archival vulvar tissues originating from 55 preoperatively untreated patients were immunostained with antibodies to survivin and γ -H2AX to determine their expression in normal squamous vulvarepithelia (NE, n=25), lichen sclerosus (n=10), high-grade classic vulvar intraepithelial neoplasia (n=16), differentiated vulvar intraepithelial neoplasia (n=16), and vulvar invasive keratinizing squamous cell carcinoma (ISCC, n=20; FIGO Ib). Immunostaining for both factors was scored for moderate and strong intensities with regard to quantity. Statistical analysis was performed by the χ test and Fisher exact test. Nuclear surviving expression increased from NE and lichen sclerosus to high-grade classic vulvar intraepithelial neoplasia, differentiated vulvar intraepithelial neoplasia, and ISCC significantly ($P=0.0001$) and followed the distribution of immature squamous epithelial cells. Positive scores for γ -H2AX were found in nuclei of cells in all diagnostic cohorts, in any epithelial level with some accentuation in the upper layers, was seen in pycnotic nuclei in horn pearls of ISCC and apoptotic bodies, without relevant statistical distributions. Immunoscoring did not differ between grade 1 and grades 2/3. Expression patterns were different for both factors, suggesting their involvement in different biologic mechanisms as an early event leading to resistance to apoptosis in vulvar carcinogenesis.

Management of vulvar intraepithelial neoplasia.

The Committee on Gynecologic Practice of the American College of Obstetricians and Gynecologists and the American Society for Colposcopy and Cervical Pathology
J Low Genit Tract Dis. 2011 Oct 19. [Epub ahead of print]

Vulvar intraepithelial neoplasia (VIN) is an increasingly common problem, particularly among women in their 40s. The term VIN is used to denote high-grade squamous lesions and is subdivided into usual-type VIN (including warty, basaloid, and mixed VIN) and differentiated VIN. Usual-type VIN is commonly associated with carcinogenic genotypes of human papillomavirus (HPV) and other HPV persistence risk factors, such as cigarette smoking and immunocompromised status, whereas differentiated VIN usually is not associated with HPV and is more often associated with vulvar dermatologic conditions, such as lichen sclerosus. Biopsy is indicated for any pigmented vulvar lesion. Treatment is indicated for all cases of VIN. When occult invasion is not a concern, VIN can be treated with surgical therapy, laser ablation, or medical therapy. After resolution, women should be monitored at 6 and 12 months and annually thereafter.