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

Vulvodynia / Vulvovaginal Pain

A manganese superoxide dismutase gene polymorphism and development of vulvar vestibulitis syndrome following physical vaginal trauma.
Lev-Sagie A, Linhares IM, Ledger WJ, Witkin SS
It J Gynacol Obstet. 2010 22 N. 2:59-64

Objective: Vulvar vestibulitis syndrome (VVS) is a disorder characterized by an inability to experience pain-free vaginal penetration. We hypothesized that one mechanism resulting in VVS was an inability to effectively inactivate reactive oxygen species that were induced by a local physical insult. Methods: VVS patients (190) and controls (194) were tested for a polymorphism at position 1183 in the manganese superoxide dismutase (MnSOD) gene. Carriage of the variant V allele is associated with reduced antioxidant activity. Results: There was no association between a diagnosis of VVS and either the V,V genotype or the allele V frequency. However, when the VVS patients were differentiated with regard to pain tolerance, carriage of the V,V genotype ($p = .019$) as well as the allele V frequency ($p = .026$) were both associated with a self-reported inability to tolerate vaginal penetration. Women whose VVS began following childbirth had the highest frequency of intolerance to vaginal penetration (9 of 13, 69.2%) as compared to all other patients (65 of 168, 38.7%) ($p = .040$). The MnSOD V,V genotype was also more frequent in women whose VVS began following an obvious vaginal trauma (childbirth or gynecological surgery (29.4%) than in women with other, or no identifiable, precipitating cause of their symptoms (10.0%) ($p = .033$). Conclusion: A decreased capacity to prevent oxidative nerve damage following a localized physical trauma due to carriage of the MnSOD gene polymorphism is associated with the onset of VVS in a subset of women.

Pelvic floor physiotherapy for women with urogenital dysfunction: indications and methods.
Rosenbaum TY
Minerva Urologica e Nefrologica. 2011 March;63(1):101-7

Pelvic floor physiotherapy (PFPT) is considered to be a salient component of the conservative management of women with urogenital dysfunction including urinary incontinence and pelvic organ prolapse (POP). PFPT is an important adjunct to the management of female pelvic and sexual pain disorders which are often associated with bothersome bladder symptoms. Physiotherapists utilize a variety of treatment methods which include behavioral therapy, exercise instruction, manual therapy, biofeedback and electrical stimulation. This review article provides a literature-based update describing and highlighting current indications and methods for pelvic floor physiotherapy intervention.

A systematic review of relationship adjustment and sexual satisfaction among women with provoked vestibulodynia.
Smith KB, Pukall CF
J Sex Res. 2011 Mar;48(2):166-91.

The main objective of this article was to conduct a systematic review of the literature examining relationship adjustment and sexual satisfaction among women with provoked vestibulodynia (PVD). Although only a small number of studies have included partners, the literature regarding partner's relationship adjustment and sexual satisfaction was also examined. Relevant articles were identified by a literature search conducted between August 2008 and May 2010. Studies were included if they contained at least one group or subset of participants with PVD or dyspareunia (i.e., painful sexual intercourse), and if they assessed relationship adjustment or sexual satisfaction as a primary outcome measure. Within this review, the methodological quality of 33 studies was systematically rated, and effect sizes were calculated when possible. Methodological type and quality greatly varied across the studies, as did the pain samples included and the outcomes reported. Nevertheless, the results of controlled studies indicate that PVD is associated with decreased sexual satisfaction. The controlled results also suggest, however, that PVD is not necessarily associated with general relationship maladjustment for women and their partners. Future research, using various methodologies, is needed to further understand intimate relationships among women with PVD and the impact that this condition may have on couples.

Genital pain in women: Beyond interference with intercourse.
Bergeron S, Rosen NO, Morin M
Pain. 2011 Feb 14. [Epub ahead of print]

No abstract available.

Prevalences of and risk factors for vulvar diseases in Nepal: a hospital-based study.
Pathak D, Agrawal S, Dhali TK
Int J Dermatol. 2011 Feb;50(2):161-7.

Background: The vulvar diseases are common skin conditions, but their frequency and importance are often underestimated. Objectives: This study is aimed to investigate the frequency and clinical patterns of vulvar diseases and the risk factors associated with these diseases in patients attending a tertiary care hospital in eastern Nepal. Methods: Patients with vulval symptoms or cutaneous lesions on the vulva were enrolled in the study. Laboratory investigations were carried out according to need. Equal numbers of age-matched females without vulval lesions or symptoms were selected from the outpatient department as controls. Results: Of 5521 female patients attending the Dermatology Department's outpatient clinic during the study period, 105 (1.9%) had vulval symptoms and/or lesions. The most common types of vulvar disease were vulvar dermatoses (62.85%), pruritus vulvae (36.19%) and vulvodynia (0.95%). In vulvar dermatoses, infection was the most common (33.4%) manifestation, with a predominance of vulvovaginal candidiasis. Other dermatoses included: cysts and tumors (5.6%); pigmentary changes (vitiligo) (5.6%); inflammatory dermatoses (6.6%); atrophic vaginitis (1.8%); erosive disease (0.9%); and dermatosis caused by sexual abuse (1.9%). Use of nylon undergarments, occasional detergent use for washing clothes, and an irregular menstrual history were found to be associated with vulvar diseases. Conclusions: Our study findings indicate that the known frequency of vulvar diseases may represent only a small proportion of actual frequency. Further clinical and population-based research should be carried out with respect to the treatment, follow-up, and true prevalence of these diseases in the community.

Tackling vulvodynia.
Nunns D
Br J Dermatol. 2011 Mar;164(3):464.

No abstract available.

Efficacy of high doses of botulinum toxin A for treating provoked vestibulodynia.
Pelletier F, Parratte B, Penz S, Moreno JP, Aubin F, Humbert P
Br J Dermatol. 2011 Mar;164(3):617-22.

Background: Provoked vestibulodynia is difficult to treat. The beneficial effects of botulinum toxin A are being considered because of the muscular anomalies observed in this pathology. Objective: To evaluate the efficacy of botulinum toxin A in the treatment of provoked vestibulodynia. Methods: Patients aged between 18 and 60 years presenting with provoked vestibulodynia (according to the 2003 International Society for the Study of Vulvar Disease classification) received 50U of botulinum toxin A bilaterally in the bulbospongiosus muscle under electromyographic monitoring. Pain was evaluated by a visual analogue scale (VAS),

quality of life was evaluated by the Dermatology Life Quality Index and sexual function by the Female Sexual Function Index. Results: Twenty patients received the injections. Sixteen patients presented with a muscular hyperactivity on electromyography. After 3 months, 80% of the patients improved in terms of pain. Mean ± SD VAS values significantly decreased from 8.37 ± 1.22 (range 4.5-10) to 2.57 ± 2.67 (0-9; P<0.0001) at month 3 and to 3.90 ± 2.92 (0-9; P<0.001) at month 6. Quality of life and sexual function improved significantly during the first 6 months (P<0.0001). After 3 months, 13 patients (out of 18 for whom intercourse was not possible before the injections; 72%) were able to have sexual intercourse. Conclusion: Botulinum toxin A seems to be an effective and safe treatment for provoked vestibulodynia; 100U botulinum toxin A significantly reduced pain 3 and 6 months after injections without side-effects. The treatment also improved quality of life and sexual function of patients. Botulinum toxin A appears to be a promising option for managing sexual pain disorder.

Successful treatment of vulvodynia with botulinum toxin a.
Tieu KD, Macgregor JL
Arch Dermatol. 2011 Feb;147(2):251-2.

No abstract available.

CT-guided percutaneous infiltration for the treatment of Alcock's Neuralgia.
Filippiadis DK, Velonakis G, Mazioti A, Alexopoulou E, Malagari A, Brountzos E, Kelekis N, Kelekis A
Pain Physician. 2011 Mar-Apr;14(2):211-5.

The pudendal nerve may be strained either between the sacrospinous and sacrotuberous ligaments at the ischial spine level or within Alcock's canal. Alcock's neuralgia is a rare, painful condition caused by compression of the pudendal nerve within Alcock's canal (pudendal canal) which is an aponeurotic tunnel that cannot be stretched. Patients usually present with intense, unilateral pain involving anatomic areas along the pudendal nerve's root, genital, anal, and pelvic regions causing mobility impairment. A computed tomography (CT) - guided percutaneous infiltration of the pudendal nerve with a mixture of a local anesthetic and a long-acting corticosteroid is a safe and efficient method that reduces the pain caused by the neuralgia. Corticosteroids and local anesthetics interfere with the neurons, the encoding, and the processing of noxious stimuli; interrupt the pain-spasm cycle; and reduce inflammation. The injected glucocorticosteroid may take 3-5 days to reach its anti-inflammatory effect; therefore, the initial pain relief from the local anesthetic is followed by a baseline pain return and then secondary pain relief at 3-5 days. The procedure is performed under minimal or no anesthesia. In general, at discharge, a responsible person must accompany the patient and ensure a safe return home. Clinical evaluation is performed after 7-10 days. There are 2 types of potential complications that are associated with percutaneous steroid infiltrations: intra-operative (associated with needle placement) and post-operative (infection, bleeding and those associated with the injectate administration). In all cases that steroids were administered

within therapeutic doses, no complications were noted. In conclusion, CT-guided percutaneous infiltration with a mixture of long-acting corticosteroid and local anesthetic seems to be a safe and efficient method for the treatment of Alcock's neuralgia.

Future indications for sacral nerve stimulation.
Dudding TC
Colorectal Dis. 2011 Mar;13 Suppl 2:23-8.

Aim: The aim of this article was to determine the effect of sacral nerve stimulation (SNS) on the treatment of faecal incontinence, constipation, irritable bowel syndrome, mixed urinary and bowel disorders, spinal injury and neurodegenerative disease, pain syndromes, and sexual dysfunction. Method: A Medline search was performed including the keywords and/or MeSH headings of 'sacral nerve stimulation', 'neuromodulation', 'artificial pacemaker', 'faecal incontinence', 'constipation' and 'anal pain'. Further studies were identified by cross-referencing from relevant articles and by appraisal of recent peer-reviewed conference abstracts and proceedings. Results: SNS has been used for the treatment of urinary, bowel and sexual dysfunction, as well as pain resulting from such disorders, and dysfunction arising from nerve injury and degenerative disease. There is a paucity of high quality evidence to support the use of SNS for the majority of novel indications at present. Conclusion: Good quality prospective, cross-over studies are required to determine the true benefits of SNS. Further research into patient selection, operative technique and stimulation parameters for existing indications will ensure a place for SNS in the future treatment algorithm of functional pelvic floor disorders.

Satisfaction and patient experience with sacral neuromodulation: results of a single center sample survey.
Leong RK, Marcelissen TA, Nieman FH, De Bie RA, Van Kerrebroeck PE, De Wachter SG
J Urol. 2011 Feb;185(2):588-92.

Purpose: We systematically assessed long-term satisfaction and patient experience with sacral nerve modulation therapy. Materials and Methods: All patients who received sacral neuromodulation between 1990 and 2007 at our center and who still had the implant were included in the survey. All received a postal questionnaire regarding satisfaction and experiences with the system, such as side effects, complications, burden, impact on sexuality and defecation changes. Results: Of the 275 questionnaires sent 207 were returned for a 75% response rate. The population was 83% female. Overall treatment was done for overactive bladder syndrome, nonobstructive urinary retention, combined overactive bladder and retention, and pelvic pain in 55%, 24%, 20% and 1% of patients, respectively. Overall satisfaction with sacral neuromodulation was high at 90%. No correlations were found between the satisfaction rate, and pretreatment age, gender, complaint type, sexual dysfunction or therapy duration. However, 56% of patients reported side effects, such as pain at the internal nerve stimulator site and due to stimulation. However, 89% of these patients did not seek

further therapy. Of patients with additional defecation problems 47% experienced relief of complaints. Conclusions: This study shows a high satisfaction rate in patients with sacral neuromodulation. There was no relation between patient age, complaint type, therapy duration or side effects and the satisfaction rate. The number of side effects was limited but further analysis in prospective cohorts should identify patients who are likely to have side effects or stop sacral neuromodulation treatment.

Characteristics of attachment style in women with dyspareunia.
Granot M, Zisman-Ilani Y, Ram E, Goldstick O, Yovell Y
J Sex Marital Ther. 2011 Jan;37(1):1-16.

In this study, the authors explored the relations among painful experience during sexual intercourse, attachment style, and somatization. The authors assessed these variables by self-report of dyspareunia (painful vaginal intercourse) and by completion of the Experience in Close Relationships Scale and the short version of the Brief Symptom Inventory. The sample included 110 women, 45 of whom reported painful intercourse and were defined as the dyspareunia group, and the remaining 65 were defined as the control group. The dyspareunia group showed greater incidence, compared with the control group, of insecure attachment styles defined by higher scores of anxiety and/or avoidance as well as higher somatization levels. Regression analyses revealed that increased level of somatization and higher level of avoidance predicted higher probability for dyspareunia. The authors' findings suggest that women with higher frequency of physical complaints in various body areas and insecure attachment style are more susceptible to report pain during intercourse.

Female sexual disorders: Assessment, diagnosis, and treatment.
Kingsberg SA, Knudson G
CNS Spectr. 2011 Feb 1. [Epub ahead of print]

Sexual health is important to overall health and quality of life. Sexual problems have been associated with relationship problems and may interfere with overall health and they may also be a marker for other undiagnosed comorbid medical conditions. In order for healthcare professionals to manage the sexual health concerns of their patients, it is important for them to understand what constitutes good sexual health. To that end, it is necessary to have a working knowledge of the evolving theoretical models offered to describe a healthy sexual response as well as an understanding of the neurobiology of sexual function. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Revised lists six primary female sexual disorders: hypoactive sexual desire disorder, sexual aversion disorder, female sexual arousal disorder, female orgasmic disorder, dyspareunia, and vaginismus. Despite a growing awareness of the high prevalence of sexual disorders they are not typically identified nor treated. There are a number of reasons why clinicians fail to identify and treat sexual problems including insufficient training in sexual medicine and communication skills, time-constraints, and embarrassment. Treatment for female sexual problems is usually individualized and may include a combination

of office-based education and basic counseling, cognitive-behavioral psychotherapy, pharmacotherapy, and treatment of concomitant medical conditions.

Resident education and training in female sexuality: results of a national survey.
Pancholy AB, Goldenhar L, Fellner AN, Crisp C, Kleeman S, Pauls R
J Sex Med. 2011 Feb;8(2):361-6.

Introduction: Considering the prevalence of female sexual dysfunction, the lack of education and training in female sexual function and dysfunction (FSF&D) during and obstetrics and gynecology residency highlights a need for greater focus on this topic. Aim: To assess understanding and confidence among third and fourth year Ob/Gyn residents with respect to FSF&D. Methods: An Internet-based survey was constructed to evaluate third and fourth year residents in American Council for Graduate Medical Education-approved Ob/Gyn programs. Residents were asked about familiarity, knowledge, and confidence in treating various aspects of FSF&D, based on the Council on Resident Education in Obstetrics and Gynecology (CREOG) Educational Objectives for Ob/Gyn training. They were also queried regarding areas of improvement for their education. Main Outcome Measure: Responses to survey instrument. Results: Two hundred thirty-four residents responded. The majority (91.5%) reported attending ≤5 didactic activities on FSF&D. Only 19.6% reported often or always screening women for sexual function problems; most had very little or no knowledge in administering or interpreting screening questionnaires. While many (82.8%) felt confident about obtaining a complete sexual history, only 54.7% felt able to perform a targeted physical exam. Although most residents had cared for women with dyspareunia (55.1%), a minority had managed many women with low desire (18.4%), arousal problems (8.1%), anorgasmia (5.6%), or vaginismus (16.7%). In treating patients, 34-56% reported rarely or never suggesting ancillary therapy such as counseling and medications. However, the majority believed that their confidence would increase through FSF&D lectures (97.9%), FSF&D patient observations (97.4%), rotating with a urogynecologist (94.4%), and online modules (90.6%). Conclusion: Despite CREOG requirements for Ob/Gyn training in female sexuality, most residents feel ill-equipped to address these problems. Additional evidence-based educational and didactic activities would enhance residents' knowledge and confidence in treating these common, quality-of-life issues

Use of the Short-Form McGill Pain Questionnaire as a diagnostic tool in women with chronic pelvic pain.
Droz J, Howard FM
J Minim Invasive Gynecol. 2011 Mar-Apr;18(2):211-7.

Study Objective: To estimate the usefulness of the Short-Form McGill Pain Questionnaire (MPQ) pain descriptors in the diagnostic evaluation of chronic pelvic pain. Design: Retrospective cohort study (Canadian Task Force classification II-2). Setting: University-based center specializing in chronic pelvic pain. Patients: Three hundred thirty-one consecutively evaluated women with chronic pelvic pain who had data sufficient for evaluation. Interventions: The

relationships between MPQ pain descriptors and subsequent diagnoses were evaluated using odds ratios, sensitivity, specificity, and positive and negative predictive values. Measurements and Main Results: The most common diagnoses were endometriosis, interstitial cystitis and painful bladder syndrome, and irritable bowel syndrome. Seventy-one percent of the patients had more than one diagnosis. Relative risks for pain descriptors as diagnostic tools for specific diagnoses were most significant, with "cramping" for endometriosis (4.0), "cramping" for interstitial cystitis and painful bladder syndrome (2.0), "sickening" for irritable bowel syndrome (1.5), and "aching" for abdominal myofascial pain syndrome (4.27). Conclusion: Several of the MPQ descriptors had high negative predictive values but not high positive predictive values, which suggests that they have diagnostic usefulness in excluding but not predicting pelvic pain-related diagnoses. This was especially the case with cramping as an MPQ descriptor in women with endometriosis. However, overall the MPQ descriptors were not robust as diagnostic tools, which suggests that inclusion of the MPQ descriptors in the evaluation of women with chronic pelvic pain is of limited diagnostic value.

Validation of the pelvic floor inventories lLeiden (PelFIs) in english.

Voorham-van der Zalm PJ, Berzuk K, Shelly B, Kamin B, Putter H, Lycklama À Nijeholt GA, Pelger RC, Stiggelbout AM

Neurourol Urodyn. 2011 Feb 23. [Epub ahead of print]

Aims: To evaluate the validity and reliability of the English translation of an interviewer-administered pelvic floor questionnaire, the "Pelvic Floor Inventories Leiden" (PeLFIs) for women, which addresses complaints of prolapse, bladder, and bowel dysfunction, pelvic floor pain and/or sexual dysfunction related to pelvic floor dysfunction. Methods: The formal forward-backward translation of the PeLFIs was performed by bilingual Dutch/English translators. The final English version was administered to healthy volunteers (N = 94) and patients (N = 180) in Canada and the United States. Psychometric properties of the English version were examined, including internal consistency, test-retest reliability, content, and construct validity. Internal consistency was measured using Cronbach's alpha. Test-retest reliability was assessed by intraclass correlation coefficients. Construct validity was established by comparing scores in healthy volunteers and patients (using t-tests) and by intercorrelating domains. Results: The forward-backward translation of the English version of the PeLFIs was consistent with the original Dutch questionnaire. In total, 274 questionnaires were administered. The retest was administered 2 weeks after the initial PeLFIs interview. Internal consistency of the questionnaire was 0.88 for the total scale. Cronbach's alpha of the domains ranged from 0.71 to 0.95. For the test-retest reliability, the agreement rate between the two tests exceeded 95% and the intraclass correlation ranged from 0.6 to 0.8. The differences between healthy volunteers and patients were statistically significant for all domains, but did not exceed the minimal important difference for some domains. Correlations between the domains were moderate to high. Conclusions: The PeLFIs questionnaire has been translated successfully into English and in its evaluation has shown adequate internal consistency and reliability.

Basic Science/Anatomy

The role of genital nerve afferents in the physiology of the sexual response and pelvic floor function.
Tajkarimi K, Burnett AL
J Sex Med. 2011 Feb 16. [Epub ahead of print]

Introduction. Our understanding of genital and pelvic floor physiology is rapidly expanding. Penile erection is a neurovascular event controlled by spinal autonomic centers, the activity of which is dependent on input from supraspinal centers and the genitalia. Genital afferent stimulation excites spinal autonomic nuclei and supraspinal sexual centers of both genders. Aim. To present a detailed understanding of the functional importance of genital afferent neuroanatomy and neurophysiology. Methods. English-written articles of diverse disciplines from 1980 to 2010 that contained information on genital anatomy, pudendal/dorsal/perineal/cavernous nerves, vibratory stimulation, reflexogenic erection, peripheral/central nervous system-mediated erectile and micturition pathways, and sexual arousal in animals and humans were reviewed. Main Outcome Measures. Analysis of supporting evidence for the role of genital afferents in the physiology of erectile response and pelvic floor function. Results. Basic science and clinical studies support the concept that pudendal nerve circuitry serves an essential purpose for sexual behavior, erectile function, penile rigidity, ejaculation, and micturition. Males and females share a comparable pattern of genital afferent neuroanatomy and neurophysiology, and sexual and micturition reflexes are similar in both genders. Pudendal nerve branches communicate with the cavernous nerves and are nitric oxide synthase positive. Genital afferents activate multiple spinal reflexes that modulate erection and micturition. Genital sensory information is transmitted to supraspinal centers important for sexual function. Conclusions. There is expanding support for the critical role of genital afferent neurophysiology in the mechanisms of erectile function and micturition. Genital afferent stimulation is a safe and natural modality that can be harnessed to amplify autonomic and somatic activity within the penis, female genitalia, spinal cord, and higher centers via established neurological principles. Such physiological adaptive processes may be beneficial in improving sexual response, erectile function, and micturition in many disease states, including in men after radical pelvic surgery. Well-designed and -executed studies in each specific population are needed to authenticate such prospects.

Neural supply to the clitoris: immunohistochemical study with three-dimensional reconstruction of cavernous nerve, spongious nerve, and dorsal clitoris nerve in human fetus.
Moszkowicz D, Alsaid B, Bessede T, Zaitouna M, Penna C, Benoit G, Peschaud F
J Sex Med. 2011. [Epub ahead of print]

Introduction. Little detailed information is available concerning autonomic and somatic nerve supply to the clitoris, potentially causing difficulties for nerve preservation during pelvic and perineal surgery. Aim. To identify the location and type (nitrergic, adrenergic, cholinergic and

sensory) of nerve fibers in the clitoris and to provide a three-dimensional (3D) representation of their structural relationship in the human female fetus. Methods. Serial transverse sections were obtained from five human female fetuses (18-31 weeks of gestation) and subjected to histological and immunohistochemical investigations; digitized serial sections were used to construct a 3D representation of the pelvis. Main Outcome Measures. Pelvic-perineal nerve location and type were evaluated qualitatively. Results. The female neurovascular bundle (NVB) is the anteroinferior terminal portion of the inferior hypogastric plexus that runs along the postero-lateral then lateral face of the vagina and is rich in nNOS-positive fibers. The cavernous nerve (CN) is a thin ventrocaudal collateral projection of the NVB, and this projection does not strictly follow the NVB course. The CN runs along the lateral surface of the vagina and urethra and penetrates the homolateral clitoral crus. The CN provides adrenergic, cholinergic, and nitrergic innervation to the clitoris, but not sensory innervation. The spongious nerve (SN) is the terminal and main projection of the NVB and provides nitrergic innervation to the vestibular bulbs. The dorsal clitoris nerve (DCN), somatic branche of the pudendal nerve, runs along the superior surface of the clitoral crus and body and has a segmental proerectile nitrergic activity related to communicating branches with the CN. Conclusions. "Computer-assisted anatomic dissection" allowed the identification of the precise location and distribution of the autonomic and somatic neural supply to female erectile bodies, providing an anatomical basis for nerve-sparing surgical techniques, and participating to the understanding of neurogenic female sexual dysfunction.

Pain

Post-traumatic stress disorder moderates the relation between documented childhood victimization and pain 30 years later.
Raphael KG, Widom CS
Pain. 2011 Jan;152(1):163-9

Cross-sectional designs and self-reports of maltreatment characterize nearly all the literature on childhood abuse or neglect and pain in adulthood, limiting potential for causal inference. The current study describes a prospective follow up of a large cohort of individuals with court-documented early childhood abuse or neglect (n=458) and a demographically matched control sample (n=349) into middle adulthood (mean age 41), nearly 30 years later, comparing the groups for risk of adult pain complaints. We examine whether Post-Traumatic Stress Disorder (PTSD) mediates or moderates risk of pain. Assessed prospectively across multiple pain measures, physically and sexually abused and neglected individuals generally showed a significant ($p<.05$) but notably small ($\eta(2)=.01$) increased risk of pain symptoms in middle adulthood. Although PTSD was associated with both childhood victimization ($p<.01$) and risk of middle adulthood pain ($p<.001$), it did not appear to mediate the relationship between victimization and pain. However, across all pain outcomes other than medically unexplained

pain, PTSD robustly interacted with documented childhood victimization to predict adult pain risk: Individuals with both childhood abuse/neglect and PTSD were at significantly increased risk ($p<.001$, $\eta(2)$ generally=.05-.06) of pain. After accounting for the combined effect of the two factors, neither childhood victimization nor PTSD alone predicted pain risk. Findings support a view that clinical pain assessments should focus on PTSD rather than make broad inquiries into past history of childhood abuse or neglect.

Efficacy of antidepressants as analgesics: A review.
Dharmshaktu P, Tayal V, Kalra BS
J Clin Pharmacol. 2011 Mar 17. [Epub ahead of print]

No abstract available.

Application of botulinum toxin in pain management.
Sim WS
Korean J Pain. 2011 Mar;24(1):1-6.

Botulinum toxin has been used for the treatment of many clinical disorders by producing temporary skeletal muscle relaxation. In pain management, botulinum toxin has demonstrated an analgesic effect by reducing muscular hyperactivity, but recent studies suggest this neurotoxin could have direct analgesic mechanisms different from its neuromuscular actions. At the moment, botulinum toxin is widely investigated and used in many painful diseases such as myofascial syndrome, headaches, arthritis, and neuropathic pain. Further studies are needed to understand the exact analgesic mechanisms, efficacy and complications of botulinum toxin in chronic pain disorders.

Factor analysis of responses to thermal, electrical, and mechanical painful stimuli supports the importance of multi-modal pain assessment.
Neziri AY, Curatolo M, Nüesch E, Scaramozzino P, Andersen OK, Arendt-Nielsen L, Jüni P
Pain. 2011 Mar 9. [Epub ahead of print]

During the last decade, a multi-modal approach has been established in human experimental pain research for assessing pain thresholds and responses to various experimental pain modalities. Studies have concluded that differences in responses to pain stimuli are mainly related to variation between individuals rather than variation in response to different stimulus modalities. In a factor analysis of 272 consecutive volunteers (137 men and 135 women) who underwent tests with different experimental pain modalities, it was determined whether responses to different pain modalities represent distinct individual uncorrelated dimensions of pain perception. Volunteers underwent single painful electrical stimulation, repeated painful electrical stimulation (temporal summation), test for reflex receptive field, pressure pain stimulation, heat pain stimulation, cold pain stimulation, and a cold pressor test (ice water

test). Five distinct factors were found representing responses to 5 distinct experimental pain modalities: pressure, heat, cold, electrical stimulation, and reflex-receptive fields. Each of the factors explained approximately 8% to 35% of the observed variance, and the 5 factors cumulatively explained 94% of the variance. The correlation between the 5 factors was near null (median ρ=0.00, range -0.03 to 0.05), with 95% confidence intervals for pairwise correlations between 2 factors excluding any relevant correlation. Results were almost similar for analyses stratified according to gender and age. Responses to different experimental pain modalities represent different specific dimensions and should be assessed in combination in future pharmacological and clinical studies to represent the complexity of nociception and pain experience. Responses to different experimental pain modalities represent different specific dimensions, supporting multimodal pain assessment for clinical and research purposes.

Breakout session: Gender and ethnic disparities in pain management.
Kamath AF, O'Connor MI
Clin Orthop Relat Res. 2011 Jan 29. [Epub ahead of print]

BACKGROUND: Pain management is a complex and evolving topic. Treatment of pain must account for biochemical as well as social and economic factors. Sex, gender, and ethnic differences exist in the pathophysiology, diagnosis, and provision of care for patients with pain. QUESTIONS/PURPOSES: We sought to identify the sex, gender, and ethnic disparities leading to care inequalities with respect to pain management. Our purposes were to (1) clarify the state of where we are now, (2) outline ways to approach where we need to go, and (3) generate solutions for how we get there. WHERE ARE WE NOW?: Studies are beginning to uncover the biologic mechanisms underlying the pain response in sex, gender, and ethnic subgroups. Patient characteristics that increase the risk of postoperative pain are being identified. WHERE DO WE NEED TO GO?: Much work needs to be done in medical education with respect to sex, gender, and ethnic disparities in pain management. Research efforts must better describe differences in physiology of pain, incidence of pain, coping strategies, patient-doctor relationships, and gender/ethnic-specific modes of care for the patient with pain. HOW DO WE GET THERE?: Future work will involve combined efforts with pain/anesthesia specialty societies, developing a disparities and pain management curriculum for medical providers, endorsing health literacy, performing high-quality Level I/II research, and exploring systems processes in pain management in the acute hospital setting.

A new program in pain medicine for medical students: integrating core curriculum knowledge with emotional and reflective development.
Murinson BB, Nenortas E, Mayer RS, Mezei L, Kozachik S, Nesbit S, Haythornthwaite JA, Campbell JN
Pain Med. 2011 Feb;12(2):186-95.

Objective: Improvements in clinical pain care have not matched advances in scientific knowledge, and innovations in medical education are needed. Several streams of evidence

indicate that pain education needs to address both the affective and cognitive dimensions of pain. Our aim was to design and deliver a new course in pain establishing foundation-level knowledge while comprehensively addressing the emotional development needs in this area. Setting: One hundred eighteen first-year medical students at Johns Hopkins School of Medicine. Outcome Measures: Performance was measured by multiple-choice tests of pain knowledge, attendance, reflective pain portfolios, and satisfaction measures. Results: Domains of competence in pain knowledge included central and peripheral pain signalling, pharmacological management of pain with standard analgesic medications, neuromodulating agents, and opioids; cancer pain, musculoskeletal pain, nociceptive, inflammatory, neuropathic, geriatric, and pediatric pain. Socio-emotional development (portfolio) work focused on increasing awareness of pain affect in self and others, and on enhancing the commitment to excellence in pain care. Reflections included observations on a brief pain experience (cold pressor test), the multidimensionality of pain, the role of empathy and compassion in medical care, the positive characteristics of pain-care role models, the complex feelings engendered by pain and addiction including frustration and disappointment, and aspirations and commitments in clinical medicine. The students completing feedback expressed high levels of interest in pain medicine as a result of the course. Discussion: We conclude that a 4-day pain course incorporating sessions with pain specialists, pain medicine knowledge, and design-built elements to strengthen emotional skills is an effective educational approach. Summary: Innovations in medical education about pain are needed. Our aim was to design and deliver a new course for medical students addressing both the affective and cognitive dimensions of pain. Combining small-group sessions with pain specialists, active-learning approaches to pain knowledge, and design-built elements to strengthen emotional skills was highly effective.

Other Vulvovaginal Disorders

Intravaginal dehydroepiandrosterone (prasterone), a highly efficient treatment of dyspareunia.
Labrie F, Archer DF, Bouchard C, Fortier M, Cusan L, Gomez JL, Girard G, Baron M, Ayotte N, Moreau M, Dubé R, Côté I, Labrie C, Lavoie L, Berger L, Gilbert L, Martel C, Balser J
Climacteric. 2011 Apr;14(2):282-8.

Objective: To examine the effect of intravaginal dehydroepiandrosterone (DHEA) on pain at sexual activity (dyspareunia) identified as the most bothersome symptom of vaginal atrophy in postmenopausal women at both screening and day 1. Methods: This prospective, randomized, double-blind and placebo-controlled phase III clinical trial studied the effect of prasterone (DHEA) applied locally in the vagina on the severity of dyspareunia in 114 postmenopausal women who had identified dyspareunia as their most bothersome symptom of vaginal atrophy, while meeting the criteria for superficial cells ≤ 5% and pH > 5.0 at both screening and day 1. Results: At the standard duration of 12 weeks of treatment, increasing doses of 0.25%, 0.5% and 1.0% DHEA decreased the percentage of parabasal cells by 48.6 ± 6.78%, 42.4 ± 7.36% and

54.9 ± 6.60% ($p < 0.0001$ vs. placebo for all) with no change with placebo ($p = 0.769$). The effects on superficial cells and pH were also highly significant compared to placebo at all DHEA doses. The severity score of pain at sexual activity decreased by 0.5, 1.4, 1.6 and 1.4 units in the placebo and 0.25%, 0.5% and 1.0% DHEA groups, respectively, with the p value of differences from placebo ranging from 0.0017 to < 0.0001. Conclusions: Intravaginal DHEA, through local estrogen and androgen formation, causes a rapid and highly efficient effect on pain at sexual activity without systemic exposure of the other tissues, thus avoiding the recently reported systemic effects of estrogens.

Safety and tolerability of testosterone patch therapy for up to 4 years in surgically menopausal women receiving oral or transdermal oestrogen.
Nachtigall L, Casson P, Lucas J, Schofield V, Melson C, Simon JA
Gynecol Endocrinol. 2011 Jan;27(1):39-48.

Two clinical trials previously demonstrated the safety of 300 μg/day transdermal testosterone patch (TTP) treatment for up to 6 months in 1094 surgically menopausal women with hypoactive sexual desire disorder (HSDD). Adverse events (AE), clinical laboratory tests, vital signs, physical examinations and mammograms were evaluated in open-label extensions of these two trials for up to 4 years and are presented in this article. Nine hundred and sixty-seven patients received at least one application of the TTP resulting in 1092 patient-years of exposure. There was no increase over time in the rate of new occurrences or severity of AEs, serious AEs, or withdrawals due to AEs. The most common AEs associated with treatment were application site reactions and unwanted hair growth; however, most were mild and rarely resulted in study withdrawal. No clinically meaningful changes in serum chemistry, haematology, lipid profile, carbohydrate metabolism, renal and liver function or coagulation parameters were noted with up to 4 years of therapy. Consistent with age-appropriate expected rates, three cases of invasive breast cancer were observed. No important changes in the safety or tolerability profile of TTP were revealed with long-term use for up to 4 years in otherwise healthy oophorectomised women with HSDD on concomitant oestrogen.

A double-blind, randomized controlled trial of clobetasol versus pimecrolimus in patients with vulvar lichen sclerosus.
Goldstein AT, Creasey A, Pfau R, Phillips D, Burrows LJ
J Am Acad Dermatol. 2011 Feb 24. [Epub ahead of print]

Background: Lichen sclerosus (LS) is a lymphocyte-mediated chronic cutaneous disorder with a predilection for the vulva. The current gold standard treatment is topical ultrapotent corticosteroids such as clobetasol. Objective: We sought to compare the safety and efficacy of clobetasol and pimecrolimus in the treatment of vulvar LS. Methods: This double-blind, randomized trial enrolled 38 women with biopsy-proven vulvar LS. This study consisted of a 2-week screening period and a 12-week treatment period. The primary efficacy variable was the change in inflammation, as determined by a dermatopathologist, on the biopsy specimens

obtained at screening and at the week 12 visit. Secondary efficacy variables included the change from baseline in pruritus and burning/pain as assessed by patients using a visual analog scale and a clinical evaluation by the investigator. Results: Clobetasol was found to be superior in improving inflammation when compared with pimecrolimus (P = .015). Both groups showed improvement in pruritus and burning/pain but this difference was not statistically significant (P = .32 and .93, respectively). Both clobetasol and pimecrolimus were found to be effective in decreasing both the total score on the Investigator Global Assessment (P = .001) and all 3 subscales. Serum levels of pimecrolimus and clobetasol did not approach levels of concern during the study period. No adverse events were reported. Limitations: This study was limited by the relatively short study duration. Conclusion: Both clobetasol and pimecrolimus appear efficacious and well tolerated for the treatment of vulvar LS; however, clobetasol is more effective than pimecrolimus and should remain first-line therapy for LS.

Cell cycle regulation and proliferation in lichen sclerosus.
Gambichler T, Kammann S, Tigges C, Kobus S, Skrygan M, Meier JJ, Köhler CU, Scola N, Stücker M, Bechara FG, Altmeyer P, Kreuter A
Regul Pept. 2011 Feb 15. [Epub ahead of print]

Introduction: Genital lichen sclerosus (LS) is considered a potential precursor lesion of squamous cell carcinoma. We aimed to investigate the expression pattern of cell cycle regulators, tumour suppressor proteins and proliferation markers in genital LS as compared to extragenital LS (ELS) and healthy controls (HC). Methods: In order to assess the expression of minichromosome maintenance protein 3 (MCM3), MCM7, Ki-67, cyclin D1, cyclin E, p16, p21, and p53, immunohistochemistry and immunofluorescence were performed on skin specimens obtained from the genital region of LS patients (short-standing LS, n=19; long-standing LS, n=15), patients with ELS (n=10), and HC (n=8). Results: Median protein expression of MCM3 and Ki-67 was significantly higher in LS when compared to ELS and HC. In patients with long-standing LS, the expression profiles of MCM3 and Ki-67 significantly correlated. Moreover, long-standing LS lesions showed significantly increased expression of p53 when compared to short-standing LS, ELS, and HS. Immunoreactivity of MCM7, p16, p21, cyclin D1 and cyclin E did not significantly differ between the groups. Conclusions: Tumour suppressor proteins such as p53 are significantly overexpressed in genital LS when compared to extragenital disease and healthy skin. The significant p53 overexpression, particularly in long-standing genital lesions, may reflect the increased risk of malignant transformation and/or oxidative stress associated with LS. Moreover, we have demonstrated that proliferation markers such as Ki-67 and MCM3 are significantly up-regulated in genital LS as compared to controls. With regard to cell cycle regulation and proliferation rates, ELS significantly differs from its genital counterpart.

Topical antineoplastic agents in the treatment of mucocutaneous diseases.
Grossberg AL, Gaspari AA
Curr Probl Dermatol. 2011;40:71-82.

Topical antineoplastic agents have a well-established role in the treatment of several dermatological conditions. Their use in the treatment of mucosal skin disease also has gained increasing recognition. Topical 5-fluorouracil (5-FU), an antimetabolite, and imiquimod, an immunomodulatory agent with antitumor properties, are the two principal topical antineoplastic agents used in the treatment of mucocutaneous diseases. Although the vast majority of their mucosal uses are currently not approved by the Federal Drug Administration, there are numerous case series, open-label studies and randomized controlled trials supporting their uses in the treatment of mucocutaneous diseases. Both topical 5-FU and imiquimod have been successfully utilized in the treatment of a wide range of mucosal diseases, including actinic cheilitis, Bowen's disease of the anal and vulvar mucosa, and genital and perianal condyloma. Reports of their uses in the treatment of mucocutaneous diseases indicate that these agents can be safely administered, though adverse effects such as local inflammation may be augmented when these agents are applied to mucosal surfaces. Additionally, locally acting intralesional chemotherapeutic agents, such as bleomycin and interferon, have well-defined applications in the treatment of mucosal skin diseases such as condyloma acuminata. As further studies are conducted, these topical and intralesional neoplastic agents, in addition to emerging agents that are in various stages of development, such as Toll-like receptor 9 agonists and ingenol mebutate, may play an increasingly important role in the future treatment of mucocutaneous diseases.

Anti-inflammatory treatment.
Fistarol SK, Itin PH
Curr Probl Dermatol. 2011;40:58-70.

Inflammatory mucosal disorders are treated conventionally with potent or superpotent topical corticosteroids. For more than 20 years, topical cyclosporine has been used in the management of oral mucous membrane affections. Recently other topically applied calcineurin inhibitors, namely tacrolimus and pimecrolimus, expanded the armamentarium for the treatment of inflammatory mucosal diseases. This chapter places its main emphasis on the efficacy and safety of topical calcineurin inhibitors in the management of different oral and genital conditions, including anogenital lichen sclerosus (LS), oral and genital lichen planus, plasma cell balanitis and vulvitis, mucous membrane pemphigoid and pemphigus vulgaris, all conditions having usually a protracted course, requiring long-lasting treatment. There is current evidence for the effectiveness of both pimecrolimus and tacrolimus in the topical treatment of inflammatory oral mucosal diseases and genital dermatoses, especially oral lichen planus and genital LS.

Topical therapy for mucosal yeast infections.
Summers PR
Curr Probl Dermatol. 2011;40:48-57.

Mucosal yeast infection is best understood as a consequence of compromised mucosal cell-mediated and innate immunity. Defense against oral candidiasis is dominantly cell mediated. The innate immune system may play the main role in regulating vulvovaginal yeast infection. Conditions that compromise cell-mediated immunity such as leukemia, severe illness and HIV infection must be considered as predisposing factors for recurrent oral candidiasis. Compromise of vaginal innate immunity due to mucosal allergy or due to a genetic defect such as mannose-binding lectin deficiency contributes to chronic vulvovaginal yeast infection. Treatment of cofactors must be considered in order to achieve control in recurrent mucosal yeast infection.

Antimicrobial topical agents used in the vagina.
Frey Tirri B
Curr Probl Dermatol. 2011;40:36-47.

Vaginally applied antimicrobial agents are widely used in the vagina in women with lower genital tract infections. An 'antimicrobial' is a general term that refers to a group of drugs that are effective against bacteria, fungi, viruses and protozoa. Topical treatments can be prescribed for a wide variety of vaginal infections. Many bacterial infections, such as bacterial vaginosis, desquamative inflammatory vaginitis or, as some European authors call it, aerobic vaginitis as well as infection with Staphylococcus aureus or group A streptococci, may be treated in this way. Candida vulvovaginitis is a fungal infection that is very amenable to topical treatment. The most common viral infections which can be treated with topical medications are condylomata acuminata and herpes simplex. The most often encountered protozoal vaginitis, which is caused by Trichomonas vaginalis, may be susceptible to topical medications, although this infection is treated systemically. This chapter covers the wide variety of commonly used topical antimicrobial agents for these diseases and focuses on the individual therapeutic agents and their clinical efficacy. In addition, potential difficulties that can occur in practice, as well as the usage of these medications in the special setting of pregnancy, are described in this chapter.

Self-elimination of risk factors for recurrent vaginal candidosis.
Donders GG, Mertens I, Bellen G, Pelckmans S
Mycoses. 2011 Jan;54(1):39-45.

Women suffering from recurrent vulvo-vaginal candidosis (RVC) often follow medical and non-medical advices to diminish the severity and frequency of the recurrences, but the impact of such interventions is unclear. The aim of this study was to identify differences in life style habits of women with RVC compared with normal women and to define which changes have influenced the frequency of recurrences in these women. Fifty-one women with RVC and 51 age-matched control women without a history of RVC were sent a questionnaire. History of allergic disease (OR 2.8) and use of corticoids (OR 5) were more frequent in patients with RVC than controls. When interrogated about beneficial changes introduced in their life style habits, lowering the intake of sugars, preventing perineum humidity and stopping contraceptive pills were factors offering substantial improvement. Apart from an increased risk of having an

allergic constitution, no differences in the medical history or life style habits were evident between women with RVC and healthy women. However, women with RVC have introduced several changes in life style habits that proved beneficial to them. Among these changes, lowering intake of sugars, preventing perineum humidity and stopping oral contraceptives were the most important.

Susceptibility profile of vaginal isolates of Candida albicans prior to and following fluconazole introduction - impact of two decades.
Bulik CC, Sobel JD, Nailor MD
Mycoses. 2011 Jan;54(1):34-8.

Current treatment options for vulvovaginal candidiasis due to Candida albicans include over-the-counter and prescription antifungal agents. Fluconazole has been used extensively with an unknown impact on susceptibility. To investigate antifungal susceptibility trends in clinical vaginal isolates of C. albicans from 1986 to 2008, microdilution susceptibility was performed on randomly selected single isolates. Minimum inhibitory concentrations (MICs) were determined for: fluconazole, clotrimazole, miconazole, ketoconazole, itraconazole, voriconazole, flucytosine and amphotericin B. The MIC(90) for each drug was then calculated for the time periods: 1986-1989, 1992-1996 and 2005-2007. A total of 250 C. albicans vaginal isolates were included. The MIC(90) (mcg ml(-1)) for fluconazole was 0.25, 0.5 and 0.5 mcg ml(-1) for each grouping, respectively. The corresponding MIC(90) for flucytosine was 1, 2 and 8 mcg ml(-1) , respectively. The MIC(90) for the remaining agents remained unchanged across time periods mentioned. Of note, the percentage of isolates with MIC ≥1 and ≥2 mcg ml(-1) for fluconazole increased from 3% to 9% over the study period. Although the C. albicans MIC(90) to fluconazole in vaginal isolates has not shown a clinically significant increase since 1986, there is an increasing number of isolates with elevated MICs. The implications of this increase are unknown, but given the achievable vaginal concentrations of fluconazole, reduced susceptibility may have clinical relevance.

Prospects for development of a vaccine to prevent and control vaginal candidiasis.
Fidel PL Jr, Cutler JE
Curr Infect Dis Rep. 2011 Feb;13(1):102-7.

A vaccine against recurrent vulvovaginal candidiasis (RVVC) would benefit a large number of women who suffer from this debilitating syndrome. To date, several antigen formulations have been tested with modest results. In this article, we review the latest vaccine study reported in the literature. The candidate is a β-glucan conjugate administered with a human compatible adjuvant. Results in a mouse model of vaginitis were again modest for protection. However, the study included live animal imaging to quantify fungal burden; animals were challenged with a Candida strain carrying a gene encoding a glycophosphatidylinositol (GPI)-linked cell wall protein and luciferase. Fungal burden was expressed as photons following substrate administration. Protection appeared to be mediated by β-glucan antibodies. Although modest

protection was observed, the imaging system was less variable than semi-quantitative plate counts of vaginal lavage fluid. Despite these advances in evaluating protection, a vaccine candidate against RVVC worthy of clinical testing remains elusive.

Patient preferences and treatment safety for uncomplicated vulvovaginal candidiasis in primary health care.

Del-Cura González I, García-de-Blas González F, Cuesta TS, Fernández JM, Del-Alamo Rodríguez JM, Escriva Ferrairo RA, Del Canto De-Hoyos Alonso M, Arenas LB, Barrientos RR, Wiesmann EC, De-Alba Romero C, Díaz YG, Rodríguez-Moñino AP, Teira BG, Del Pozo MS, Horcajuelo JF, Rojas Giraldo MJ, González PC, Vello Cuadrado RA, Uriarte BL, Yepes JS, Sanz YH, Iglesias Piñeiro MJ, Hernández ST, Alonso FG, González González AI, Fernández AS, Carballo C, López AR, Morales F, Martínez López D, GRUPO PRESEVAC

BMC Public Health. 2011 Jan 31;11:63.

Background: Vaginitis is a common complaint in primary care. In uncomplicated candidal vaginitis, there are no differences in effectiveness between oral or vaginal treatment. Some studies describe that the preferred treatment is the oral one, but a Cochrane's review points out inconsistencies associated with the report of the preferred way that limit the use of such data. Risk factors associated with recurrent vulvovaginal candidiasis still remain controversial. Methods/Design: This work describes a protocol of a multicentric prospective observational study with one year follow up, to describe the women's reasons and preferences to choose the way of administration (oral vs topical) in the treatment of not complicated candidal vaginitis. The number of women required is 765, they are chosen by consecutive sampling. All of whom are aged 16 and over with vaginal discharge and/or vaginal pruritus, diagnosed with not complicated vulvovaginitis in Primary Care in Madrid.The main outcome variable is the preferences of the patients in treatment choice; secondary outcome variables are time to symptoms relief and adverse reactions and the frequency of recurrent vulvovaginitis and the risk factors. In the statistical analysis, for the main objective will be descriptive for each of the variables, bivariant analysis and multivariate analysis (logistic regression).. The dependent variable being the type of treatment chosen (oral or topical) and the independent, the variables that after bivariant analysis, have been associated to the treatment preference. Discussion: Clinical decisions, recommendations, and practice guidelines must not only attend to the best available evidence, but also to the values and preferences of the informed patient.

Plant production of anti-β-glucan antibodies for immunotherapy of fungal infections in humans.

Capodicasa C, Chiani P, Bromuro C, De Bernardis F, Catellani M, Palma AS, Liu Y, Feizi T, Cassone A, Benvenuto E, Torosantucci A

Plant Biotechnol J. 2011 Jan 25. [Epub ahead of print]

There is an increasing interest in the development of therapeutic antibodies (Ab) to improve the control of fungal pathogens, but none of these reagents is available for clinical use. We

previously described a murine monoclonal antibody (mAb 2G8) targeting β-glucan, a cell wall polysaccharide common to most pathogenic fungi, which conferred significant protection against Candida albicans, Aspergillus fumigatus and Cryptococcus neoformans in animal models. Transfer of this wide-spectrum, antifungal mAb into the clinical setting would allow the control of most frequent fungal infections in many different categories of patients. To this aim, two chimeric mouse-human Ab derivatives from mAb 2G8, in the format of complete IgG or scFv-Fc, were generated, transiently expressed in Nicotiana benthamiana plants and purified from leaves with high yields (approximately 50 mg Ab/kg of plant tissues). Both recombinant Abs fully retained the β-glucan-binding specificity and the antifungal activities of the cognate murine mAb against C. albicans. In fact, they recognized preferentially β1,3-linked glucan molecules present at the fungal cell surface and directly inhibited the growth of C. albicans and its adhesion to human epithelial cells in vitro. In addition, both the IgG and the scFv-Fc promoted C. albicans killing by isolated, human polymorphonuclear neutrophils in ex vivo assays and conferred significant antifungal protection in animal models of systemic or vulvovaginal C. albicans infection. These recombinant Abs represent valuable molecules for developing novel, plant-derived immunotherapeutics against candidiasis and, possibly, other fungal diseases.

The epidemiology of Candida species associated with vulvovaginal candidiasis in an Iranian patient population.

Mahmoudi Rad M, Zafarghandi S, Abbasabadi B, Tavallaee M

Eur J Obstet Gynecol Reprod Biol. 2011 Apr;155(2):199-203.

Objectives: Vulvovaginal candidiasis is a common infection among women worldwide. According to previous epidemiological studies, Candida albicans is the most common species of Candida. The prevalence of non-Candida species, however, is increasing. Identification of Candida species among the population will not only help health professionals to choose suitable antifungal treatments, but also prevent development of drug resistance. The aim of this study was to identify, using chromogenic agar medium, the Candida species associated with vulvovaginal candidiasis among a sample of the Iranian population. Study Design: In a prospective cohort study during a two year period from March 2006 to March 2008, swab samples of vaginal discharge/secretion were taken from 200 patients admitted to the gynecology clinic of Mahdieh Hospital (Tehran, Iran) with a clinical presentation suggestive of vulvovaginal candidiasis. The isolates obtained were cultured on Sabouraud dextrose agar and chromogenic agar medium. Candida species were also identified by germ tube formation in serum, chlamydospore production on Corn Meal Agar and carbohydrate absorption using the API 20C-AUX kit. Participants were asked to complete a questionnaire investigating the risk factors associated with candidiasis. An assessment of the different species of recurrent and non-recurrent candidiasis was also made. Descriptive statistics, chi-square test, and t-test were used to analyze the data. Results: A total of 191 isolates were obtained from 175 vaginal specimens. Candida albicans accounted for 67% of the strains including single and mixed infections. The other identified species were Candida glabrata (18.3%), Candida tropicalis (6.8%), Candida krusei (5.8%), Candida parapsilosis (1.6%), and Candida guilliermondii (0.5%)

respectively. Mixed infection with two or more species of Candida was seen in 10.3% of patients. The most common mixed cause was the combination of Candida albicans and Candida glabrata. Participants who were sexually active and those who had orogenital sex were more likely to suffer recurrent vulvovaginal candidiasis. Conclusions: Candida albicans was the most common cause of recurrent and non-recurrent vulvovaginitis. The second most common species was Candida glabrata. This study suggests CHROMagar method as a convenient and cost effective yet reliable method to isolate the species of Candida especially in cases where more than one species is present.

Group A streptococcal vaginitis: an unrecognized cause of vaginal symptoms in adult women.
Verstraelen H, Verhelst R, Vaneechoutte M, Temmerman M
Arch Gynecol Obstet. 2011 Feb 19. [Epub ahead of print]

Purpose: Vaginal infection with group A streptococci (GAS) is an established cause of vaginitis amongst prepubescent girls, but largely unrecognized in adult women and therefore often misdiagnosed as vulvovaginal candidosis. We sought to give an overview of the epidemiology, risk factors, symptoms, signs, and treatment of GAS vaginitis in adult women. Methods: Systematic literature search. Results: We identified nine case reports covering 12 patients with documented GAS vulvovaginitis. GAS vulvovaginitis in adult women is often associated with a predisposing factor: (1) household or personal history of dermal or respiratory infection due to GAS, (2) sexual contact, and (3) lactational or menopausal vaginal atrophy. Symptoms of GAS vulvovaginitis in adult women may include vaginal and/or vulvar pain, dyspareunia, burning sensation or irritation, and pruritus. In most cases, there is also profuse or copious vaginal discharge which may be watery, yellow, or even purulent. Whilst there are neither clinical trials nor treatment guidelines, treatment with oral penicillin or with vaginal clindamycin cream has been reported to result in rapid cure. In breast-feeding and postmenopausal women with vaginal atrophy, additional treatment with local estriol may be necessary to prevent recurrence. Finally, in case of recurrent GAS vulvovaginitis it will be necessary to assess the patients' asymptomatic household members for pharyngeal and anal carriage and to treat them accordingly. Conclusion: Vaginal infection with GAS in adult women is a clearly defined entity and should be considered a diagnosis when more common causes of vaginitis have been ruled out.

Lack of Candida africana and Candida dubliniensis in Vaginal Candida albicans Isolates in Turkey Using HWP1 Gene Polymorphisms.
Gumral R, Sancak B, Guzel AB, Saraçlı MA, Ilkit M
Mycopathologia. 2011 Mar 6. [Epub ahead of print]

Candida africana differs from the common strains of C. albicans and C. dubliniensis morphologically, physiologically, genetically, and, in particular, clinically. This fungal pathogen is primarily recovered from genital specimens, especially in vaginal specimens. In this investigation, we reexamined 195 vaginal C. albicans isolates for the presence of C. africana and

C. dubliniensis by using hyphal wall protein 1 (HWP1) gene polymorphisms. All study isolates were confirmed to be C. albicans, and none were verified as either C. africana or C. dubliniensis. In conclusion, the HWP1 gene polymorphisms offer a useful tool in the discrimination of C. africana, C. albicans, and C. dubliniensis. Further studies may highlight the pathogenesis and importance of this yeast in vulvovaginal candidiasis.

Anogenital malignancies and pre-malignancies.
Henquet C
J Eur Acad Dermatol Venereol. 2011 Jan 28. [Epub ahead of print]

Anogenital pre-malignancies and malignancies are frequently encountered. Aetiopathogenetically, human papillomavirus (HPV) infection plays a critical role. However, there is a variable degree of association of HPV infection with the development of anogenital malignancies. In this context, the high level of clinically unapparent HPV infection should be considered. Therefore, the question arises if the association with HPV is always causative. Besides HPV, pre-existent lichen sclerosus is also an important aetiopathologic factor in the development of anogenital malignancies. Common anogenital pre-malignancies comprise Bowen's disease (BD), Bowenoid papulosis (BP) and erythroplasia of Queyrat (EQ). From a clinical point of view, these are clearly different entities, but from a histopathological point of view, BD, BP and EQ are indistinguishable. They all represent forms of squamous intraepithelial neoplasia (IN). Intraepithelial neoplasia (IN) is not only restricted to squamous variants, but also includes non-squamous IN, Paget's disease (PD) and melanoma in situ. The risk of developing anogenital (pre)malignancies or other tumours is higher in immunocompromised and immunodeficient patients, in particular those suffering from human immunodeficiency virus (HIV) infection. Such risk factors will affect treatment and follow-up modalities. Regarding prophylactic measures, a relatively recent but very important development is the availability of HPV vaccination on a large scale. Momentarily, the effects of such vaccination, on a population-based scale, are not yet clear but will become apparent in the near future. Management of anogenital pre-malignancies and malignancies should be tailor-made and may be organized in a multidisciplinary fashion.