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Vulvodynia / Vulvovaginal Pain

Pelvic floor muscle assessment outcomes in women with and without provoked vestibulodynia and the impact of a physical therapy program.
Gentilcore-Saulnier E, McLean L, Goldfinger C, Pukall CF, Chamberlain S.
J Sex Med. 2010 Jan 6. [Epub ahead of print]

ABSTRACT Introduction. Physical therapy (PT) may reduce the pain associated with provoked vestibulodynia (PVD) based on previous findings that pelvic floor muscle dysfunction (PFMD) is associated with PVD symptoms. Aims. The goals of this study were: (i) to determine whether women with and without PVD differ on measures of pelvic floor muscle (PFM) behavior; and (ii) to assess the impact of PT treatment for women with PVD on these measures. Methods. Eleven women with PVD and 11 control women completed an assessment evaluating PFM behavior using surface electromyography (SEMG) recordings and a digital intravaginal assessment. Women with PVD repeated the assessment after they had undergone eight PT treatment sessions of manual therapy, biofeedback, electrical stimulation, dilator insertions, and home exercises. Main Outcome Measures. Superficial and deep PFM SEMG tonic activity and phasic activity in response to a painful pressure stimulus, PFM digital assessment variables (tone, flexibility, relaxation capacity, and strength). Results. At pretreatment, women with PVD had higher tonic SEMG activity in their superficial PFMs compared with the control group, whereas no differences were found in the deep PFMs. Both groups demonstrated contractile responses to the painful pressure stimulus that were significantly higher in the superficial as compared with the deep PFMs, with the responses in the PVD group being higher than those in control women. Women with PVD had higher PFM tone, decreased PFM flexibility and lower PFM relaxation capacity compared with control women. Posttreatment improvements included less PFM responsiveness to pain, less PFM tone, improved vaginal flexibility, and improved PFM relaxation capacity, such that women with PVD no longer differed from controls on these measures. Conclusion. Women with PVD demonstrated altered PFM behavior when compared with controls, providing empirical evidence of PFMD, especially at the superficial layer. A PT rehabilitation program specifically targeting PFMD normalized PFM behavior in women with PVD. Gentilcore-Saulnier, E, McLean L, Goldfinger C, Pukall CF, and Chamberlain S. Pelvic floor muscle assessment outcomes in women with and without provoked vestibulodynia and the impact of a physical therapy program.

Moving beyond the diagnosis of vestibulodynia--a holiday wish list.
Goldstein AT.
J Sex Med. 2009 Dec;6(12):3227-9.
No abstract available.

Can oral contraceptives cause vestibulodynia?
Goldstein A, Burrows L, Goldstein I.
J Sex Med. 2010 Jan 25. [Epub ahead of print]

ABSTRACT Aim. To describe the clinical course of a young woman who developed vestibulodynia with introital dyspareunia while on oral contraceptive (OCs) and to provide a possible explanation for the etiology of her symptoms as well as her recovery after treatment. Methods. A single case is presented including subjective reporting, laboratory evaluation, and quantitative sensory testing. Results. After topical hormonal therapy, the patient reported resolution of her dyspareunia and her laboratory values normalized.

Impact of educational seminars on women with provoked vestibulodynia.
Brotto LA, Sadownik L, Thomson S.
J Obstet Gynaecol Can. 2010 Feb;32(2):132-8.

Objective: Provoked vestibulodynia (PVD) is a common genital pain condition characterized by severe pain upon vaginal penetration. The treatment of women with PVD suggests variable efficacy across modalities. The emotional toll of PVD, because of the intimate and interpersonal nature of this sexually-provoked pain, and the relationship between PVD and anxiety, depression, and a host of subclinical emotional symptoms that may interfere with treatment, has been well documented. The role of the gynaecologist in identifying and managing these psychological symptoms has never been addressed. The goal of this study was to examine the efficacy of a brief, gynaecologist-led educational seminar on measures of psychological symptoms and sexual health. Methods: Twenty-nine women with PVD participated in three one-hour educational seminars led by a gynaecologist with expertise in the management of PVD. Participants completed questionnaires before, immediately after, and six months after the third session. Results: There were significant improvements in psychological symptoms of depression, anxiety, somatization, hostility, paranoid ideation, psychoticism, and the global severity index, both immediately post-seminar and at the six-month follow-up. Sexual arousal, orgasm, overall sexual function, and sexual distress also significantly improved in response to the seminars. Conclusion: Gynaecologist-led educational seminars delivered in a group format have a significant positive impact on psychological symptoms and sexual functioning in women who suffer from PVD.

Botulinum neurotoxin type a injections for vaginismus secondary to vulvar vestibulitis syndrome.
Bertolasi L, Frasson E, Cappelletti JY, Vicentini S, Bordignon M, Graziottin A.
Obstet Gynecol. 2009 Nov;114(5):1008-16.

OBJECTIVE: To investigate whether botulinum neurotoxin type A improves vaginismus and study its efficacy with repeated treatments. METHODS: Outpatients were referred because standard cognitive-behavioral and medical treatment for vaginismus and vulvar vestibular syndrome failed. From this group, we prospectively recruited consecutive women (n=39) whose diagnostic electromyogram (EMG) recordings from the levator ani muscle showed hyperactivity at rest and reduced inhibition during straining. These women were followed for a mean (+/-standard deviation) of 105 (+/-50) weeks. Recruited patients underwent repeated cycles of botulinum neurotoxin type A injected into the levator ani under EMG guidance and EMG monitoring thereafter. At enrollment and 4 weeks after each cycle, women were asked about sexual intercourse; underwent EMG evaluation and examinations to grade vaginal resistance according to Lamont; and completed a visual analog scale (VAS) for pain, the Female Sexual Function Index Scale, a quality-of-life questionnaire (Short-Form 12 Health Survey), and bowel and bladder symptom assessment. RESULTS: At 4 weeks after the first botulinum neurotoxin type A cycle,

the primary outcome measures (the possibility of having sexual intercourse, and levator ani EMG hyperactivity) both improved, as did the secondary outcomes, Lamont scores, VAS, Female Sexual Function Index Scales, Short-Form 12 Health Survey, and bowel-bladder symptoms. These benefits persisted through later cycles. When follow-up ended, 63.2% of the patients completely recovered from vaginismus and vulvar vestibular syndrome, 15.4% still needed reinjections (censored), and 15.4% had dropped out. CONCLUSION: Botulinum neurotoxin type A is an effective treatment option for vaginismus secondary to vulvar vestibular syndrome refractory to standard cognitive-behavioral and medical management. After patients received botulinum neurotoxin type A, their sexual activity improved and reinjections provided sustained benefits. LEVEL OF EVIDENCE: III.

Retrospective chart review of vaginal diazepam suppository use in high-tone pelvic floor dysfunction.
Rogalski MJ, Kellogg-Spadt S, Hoffmann AR, Fariello JY, Whitmore KE.
Int Urogynecol J Pelvic Floor Dysfunct. 2010 Jan 12. [Epub ahead of print]

To study intravaginal diazepam suppositories as adjunctive treatment for high-tone pelvic floor dysfunction (HTPFD) and sexual pain. A retrospective chart review was conducted on 26 patients who received diazepam suppositories as adjuvant therapy to pelvic physical therapy and intramuscular trigger point injections for bladder pain, sexual pain, and levator hypertonus. Pelvic floor muscular tone and pain were assessed by palpation and perineometry; sexual pain was objectively rated by Female Sexual Function Index (FSFI) and the Visual Analog Scale for Pain (VAS-P). Twenty-five out of 26 patients reported subjective improvement with suppository use; six out of seven sexually active patients resumed intercourse. Sexual pain as assessed on FSFI and serial VAS-P improved with diazepam (by 1.44 on 10-point scale, $p = 0.14$). PFM tone improved during resting ($p < 0.001$), squeezing ($p = 0.014$), and relaxation ($p = 0.003$) phases. Vaginal diazepam suppositories gave a clinically significant improvement in the treatment of HTPFD compared with the usual treatment regimen alone.

Importance of pelvic muscle tenderness evaluation in women with chronic pelvic pain.
de Souza Montenegro ML, Mateus-Vasconcelos EC, Silva JC, Nogueira AA, Dos Reis FJ, Poli Neto OB.
Pain Med.. [Epub ahead of print]

Objective. To determine the prevalence of pelvic muscle tenderness in women with chronic pelvic pain (CPP) and to assess the importance of evaluating muscle tenderness in such women. Design. Observational study of 48 healthy female volunteers and 108 women with CPP, who were clinically evaluated for pelvic muscle tenderness by two researchers blinded to all clinical data. Results. The frequency of clinically detected pelvic muscle tenderness was significantly higher in women with CPP than in healthy volunteers (58.3% vs 4.2%, $P < 0.001$). Among women with CPP, those with pelvic muscle tenderness had higher Beck Depression Index scores (22 [6-42] vs 13 [3-39], $P = 0.02$) and higher rates of dyspareunia (63.5% [40/63] vs 28.9% [13/45], $P < 0.004$) and constipation (46.0% [29/63] vs 26.7% [12/45], $P = 0.05$) than those without pelvic muscle tenderness. Conclusion. Tenderness of pelvic muscles was highly prevalent among women with CPP and was associated with higher BDI scores and higher rates of dyspareunia and constipation. Determination of pelvic muscle tenderness may help in identifying women who require more intense treatment for CPP.

Effects of high-velocity, low-amplitude spinal manipulation on strength and the basal tonus of female pelvic floor muscles.
Nogueira de Almeida BS, Sabatino JH, Giraldo PC.
J Manipulative Physiol Ther. 2010 Feb;33(2):109-116.

OBJECTIVE: Spinal manipulation with high-velocity and low-amplitude (HVLA) manipulation is frequently used for the treatment of lumbopelvic pain; however, the effect on the pelvic floor has been poorly studied in the past. The objective of this study was to quantify the intravaginal pressure (IVP) and the basal perineal tonus (BPT), measured in terms of pressure, before and after the HVLA manipulation in patients

without neuromuscular and skeletal dysfunctions. METHODS: In this experimental, noncontrolled, nonrandomized study, IVP was obtained through a perineometer introduced into the volunteers' vagina while in dorsal horizontal decubitus. Forty young, healthy university volunteer women with no history of vaginal delivery participated. All voluntary contractions of the perineal muscles were measured in 3 different ways: phasic perineal contraction (PPC), tonic perineal contraction, and perineal contraction associated to accessory muscles. New pressure measurements were obtained immediately after the HVLA manipulation on the volunteers' sacrum. The pressures were registered and transcribed directly to a personal computer with specific software. RESULTS: The average IVPs obtained in millimeters of mercury before and after the HVLA manipulation were 56.01 (+/-25.54) and 64.65 (+/-25.63) for PPC, 445.90 (+/-186.84) and 483.14 (+/-175.29) for tonic perineal contraction, and 65.62 (+/-26.56) and 69.37 (+/-25.26) for perineal contraction associated to accessory muscles, respectively. There was significant statistical variation only for PPC (P = .0020) values. The BPT increased regardless of the type of contraction (P < .05). CONCLUSION: High-velocity and low-amplitude manipulation of the sacrum was associated with an increase of PPC and of BPT in women who had no associated osteoarticular diseases. These preliminary discoveries could be helpful in the future study of the treatment of women with perineal hypotony.

Pudendal neuralgia.
Hibner M, Desai N, Robertson LJ, Nour M.
J Minim Invasive Gynecol. 2010 Jan 11. [Epub ahead of print]

Pudendal neuralgia is a painful, neuropathic condition involving the dermatome of the pudendal nerve. This condition is not widely known and often unrecognized by many practitioners. The International Pudendal Neuropathy Association (tipna.org) estimates the incidence of this condition to be 1/100,000; however, most practitioners treating patients with this condition feel the actual rate of incidence may be significantly higher. Currently, there is fair paucity of medical literature and scientific evidence in the diagnosis and treatment of pudendal neuralgia. Diagnosis of this condition is based on the utilization of Nantes Criteria, in conjunction with clinical history and physical findings. CT-scan guided nerve blocks are also employed, by this author, to provide additional information. Subsequent treatment of pudendal neuralgia is medical and well as surgical, with Physical Therapy a key component to all aspects of treatment. The goal of this paper is to present evidence based information, as well as personal clinical experience, in treating approximately 200 patients with pudendal neuralgia.

Pudendal nerve neuromodulation with neurophysiology guidance: a potential treatment option for refractory chronic pelvi-perineal pain.
Carmel M, Lebel M, Tu LM.
Int Urogynecol J Pelvic Floor Dysfunct. 2009 Dec 12. [Epub ahead of print]

Refractory chronic pelvi-perineal pain (RCPPP) is a challenging entity that has devastating consequences for patient's quality of life. Many etiologies have been proposed including pudendal neuralgia. Multiple treatment options are used but the reported results are sub-optimal and temporary. In this article, we present the technique of pudendal nerve neuromodulation with neurophysiology guidance as a treatment option for RCPPP. This technique is a two-step procedure that includes electrode implantation under neurophysiology guidance followed by the implantation of a permanent generator after a successful trial period. We report the cases of three women who underwent this procedure as a last-resort treatment option. After 2 years of follow-up, their symptoms are still significantly improved. No major complication occurred.

Women's sexual pain disorders.
van Lankveld JJ, Granot M, Weijmar Schultz WC, Binik YM, Wesselmann U, Pukall CF, Bohm-Starke N, Achtrari C.
J Sex Med. 2010 Jan;7(1 Pt 2):615-31.

INTRODUCTION: Women's sexual pain disorders include dyspareunia and vaginismus and there is need for state-of-the-art information in this area. AIM: To update the scientific evidence published in 2004, from the 2nd International Consultation on Sexual Medicine pertaining to the diagnosis and treatment of women's sexual pain disorders. METHODS: An expert committee, invited from six countries by the 3rd International Consultation, was comprised of eight researchers and clinicians from biological and social science disciplines, for the purpose of reviewing and grading the scientific evidence on nosology, etiology, diagnosis, and treatment of women's sexual pain disorders. MAIN OUTCOME MEASURE: Expert opinion was based on grading of evidence-based medical literature, extensive internal committee discussion, public presentation, and debate. Results. A comprehensive assessment of medical, sexual, and psychosocial history is recommended for diagnosis and management. Indications for general and focused pelvic genital examination are identified. Evidence-based recommendations for assessment of women's sexual pain disorders are reviewed. An evidence-based approach to management of these disorders is provided. CONCLUSIONS: Continued efforts are warranted to conduct research and scientific reporting on the optimal assessment and management of women's sexual pain disorders, including multidisciplinary approaches.

Summary of the recommendations on sexual dysfunctions in women.
Basson R, Wierman ME, van Lankveld J, Brotto L.
J Sex Med. 2010 Jan;7(1 Pt 2):314-26.

INTRODUCTION: Women's sexual dysfunction includes reduced interest/incentives for sexual engagement, difficulties with becoming subjectively and/or genitally aroused, difficulties in triggering desire during sexual engagement, orgasm disorder, and sexual pain. AIM: To update the recommendations published in 2004, from the 2nd International Consultation on Sexual Medicine (ICSM) pertaining to the diagnosis and treatment of women's sexual dysfunctions. METHODS: A third international consultation in collaboration with the major sexual medicine associations assembled over 186 multidisciplinary experts from 33 countries into 25 committees. Twenty one experts from six countries contributed to the Recommendations on Sexual Dysfunctions in Women. MAIN OUTCOME MEASURE: Expert opinion was based on grading of evidence-based medical literature, widespread internal committee discussion, public presentation, and debate. RESULTS: A comprehensive assessment of medical, sexual, and psychosocial history is recommended for diagnosis and management. Indications for general and focused pelvic genital examination are identified. Evidence based recommendations for further revisions of definitions for sexual disorders are given. An evidence based approach to management is provided. Extensive references are provided in the full ICSM reports. CONCLUSIONS: There remains a need for more research and scientific reporting on the optimal management of women's sexual dysfunctions including multidisciplinary approaches.

Sexual dysfunctions and difficulties in Denmark: prevalence and associated sociodemographic factors.
Christensen BS, Grønbæk M, Osler M, Pedersen BV, Graugaard C, Frisch M.
Arch Sex Behav. 2010 Feb 19. [Epub ahead of print]

Sexual dysfunctions and difficulties are common experiences that may impact importantly on the perceived quality of life, but prevalence estimates are highly sensitive to the definitions used. We used questionnaire data for 4415 sexually active Danes aged 16-95 years who participated in a national health and morbidity survey in 2005 to estimate the prevalence of sexual dysfunctions and difficulties and to identify associated sociodemographic factors. Overall, 11% (95% CI, 10-13%) of men and 11% (10-13%) of women reported at least one sexual dysfunction (i.e., a frequent sexual difficulty that was perceived as a problem) in the last year, while another 68% (66-70%) of men and 69% (67-71%) of women reported

infrequent or less severe sexual difficulties. Estimated overall frequencies of sexual dysfunctions among men were: premature ejaculation (7%), erectile dysfunction (5%), anorgasmia (2%), and dyspareunia (0.1%); among women: lubrication insufficiency (7%), anorgasmia (6%), dyspareunia (3%), and vaginismus (0.4%). Highest frequencies of sexual dysfunction were seen in men above age 60 years and women below age 30 years or above age 50 years. In logistic regression analysis, indicators of economic hardship in the family were positively associated with sexual dysfunctions, notably among women. In conclusion, while a majority of sexually active adults in Denmark experience sexual difficulties with their partner once in a while, approximately one in nine suffer from frequent sexual difficulties that constitute a threat to their well-being. Sexual dysfunctions seem to be more common among persons who experience economic hardship in the family.

Correlates of sexual functioning in Italian menopausal women.
Sarti CD, Graziottin A, Mincigrucci M, Ricci E, Chiaffarino F, Bonaca S, Becorpi A, Cipriani S, Parazzini F.
Climacteric. 2010 Feb 10. [Epub ahead of print]

Objectives To analyze the sexuality of Italian menopausal women. Design Cross-sectional study. Population Menopausal women consecutively observed during the study period in menopause clinics. Methods Women were interviewed about their current and premenopausal sexual activity: sexual intercourse frequency and self-rated sexual desire, capacity for orgasm and sexual satisfaction were recorded. Women were defined as having poor sexual functioning if they had one or less sexual intercourses per week or answered 'absent/poor' to the questions about the sexual domains. Results Oral hormone therapy (HT) use (odds ratio (OR) 0.43 for desire, 0.54 for orgasm and 0.56 for overall sexual satisfaction, all $p < 0.001$) and transdermal HT (OR 0.38, 0.53 and 0.53, respectively, all $p < 0.001$) were significantly associated with lower risk of poor sexual functioning. Higher physical and mental component scores (PCS and MCS, range 0-100) of the Short Form-12 are inversely related to poor sexual functioning (OR by point 0.96, 0.95, 0.95 for PCS and 0.96, 0.96 and 0.95, for MCS, respectively, all $p < 0.001$). Pain during and symptoms after sexual intercourse were significantly related to desire (OR 1.96 and 1.78, respectively), orgasm (OR 2.22 and 2.06, respectively) and sexual satisfaction (OR 2.02 and 1.79, respectively). The partner's health problems were associated with low sexual intercourse frequency (OR 4.18, $p < 0.001$) and absent/poor overall satisfaction (OR 2.61, $p < 0.001$). Conclusions This study shows that, in menopausal Italian women attending menopause clinics, sexual function is associated with the quality of sexual life in reproductive age, partner's health status, current quality of life, HT and occurrence of pain during and symptoms after sexual intercourse.

Visual attention to erotic images in women reporting pain with intercourse.
Lykins AD, Meana M, Minimi J.
J Sex Res. 2010 Jan 13:1-10. [Epub ahead of print]

The coupling of sex and pain creates an interesting theoretical conundrum of clinical significance: Are women with dyspareunia distracted from sexual stimuli, or are they hypervigilant to sexual stimuli because these stimuli elicit thoughts and expectations of pain? This study measured attention to sexual stimuli in women reporting persistent pain with intercourse, women reporting low sexual desire, and women reporting no sexual problems. Participants viewed a series of erotic images, each containing an object intended to distract from the erotic scene regions, while an eye tracker recorded their eye movements. Women with pain looked for shorter periods of time and fewer times at the sexual scene region than did both women with low sexual desire ($p = .024$ and $p = .018$, respectively) and the no-dysfunction control group ($p < .001$ and $p = .003$, respectively). Women with pain also looked at the context (nonsexual) scene region significantly more times and for longer periods than did the no-dysfunction control women ($p = .013$ and $p = .042$, respectively). Results are interpreted to be potentially supportive of the cognitive distraction hypothesis associated with sexual dysfunction, with an additional component of cognitive avoidance of sexual stimuli for the women reporting sexual pain.

Pain

Access to pain treatment as a human right.
Lohman D, Schleifer R, Amon JJ.
BMC Med. 2010 Jan 20;8:8.

ABSTRACT: BACKGROUND: Almost five decades ago, governments around the world adopted the 1961 Single Convention on Narcotic Drugs which, in addition to addressing the control of illicit narcotics, obligated countries to work towards universal access to the narcotic drugs necessary to alleviate pain and suffering. Yet, despite the existence of inexpensive and effective pain relief medicines, tens of millions of people around the world continue to suffer from moderate to severe pain each year without treatment. DISCUSSION: Significant barriers to effective pain treatment include: the failure of many governments to put in place functioning drug supply systems; the failure to enact policies on pain treatment and palliative care; poor training of healthcare workers; the existence of unnecessarily restrictive drug control regulations and practices; fear among healthcare workers of legal sanctions for legitimate medical practice; and the inflated cost of pain treatment. These barriers can be understood not only as a failure to provide essential medicines and relieve suffering but also as human rights abuses. SUMMARY: According to international human rights law, countries have to provide pain treatment medications as part of their core obligations under the right to health; failure to take reasonable steps to ensure that people who suffer pain have access to adequate pain treatment may result in the violation of the obligation to protect against cruel, inhuman and degrading treatment.

Pain channelopathies.
Cregg R, Momin A, Rugiero F, Wood JN, Zhao J.
J Physiol. 2010 Feb 22. [Epub ahead of print]

Pain remains a major clinical challenge, severely afflicting around six per cent of the population at any one time. Channelopathies that underlie monogenic human pain syndromes are of great clinical relevance, as cell surface ion channels are tractable drug targets. The recent discovery that loss of function mutations in the sodium channel Nav1.7 underlies a recessive pain free state in otherwise normal people is particularly significant. Deletion of channel-encoding genes in mice has also provided insights into mammalian pain mechanisms. Ion channels expressed by immune system cells (e.g. P2X7) have been shown to play a pivotal role in changing pain thresholds, whilst channels involved in sensory transduction (e.g. TRPV1), the regulation of neuronal excitability (Potassium channels), action potential propagation (Sodium channels) and neurotransmitter release (Calcium channels) have all been shown to be potentially selective analgesic drug targets in some animal pain models. Migraine and visceral pain have also been associated with voltage-gated ion channel mutations. Insights into such channelopathies thus provide us with a number of potential targets to control pain.

Delta and kappa opioid receptors as suitable drug targets for pain.
Vanderah TW.
Clin J Pain. 2010 Jan;26 Suppl 10:S10-5.

Similar to mu opioid receptors, kappa and delta opioid receptors reside in the periphery, the dorsal root ganglion, the spinal cord, and in supraspinal regions associated with pain modulation. Both delta and kappa opioid agonists have been shown to activate pain inhibitory pathways in the central nervous system. Yet, currently there are only a few pharmacologic agents that target kappa receptors, and none that target delta receptors. Spurred by the need for an efficacious analgesic without the unwanted side effects associated with the typical clinical profile of mu opioid agonists, new research has provided insight into why the development of effective kappa and delta opioid receptor agonists has remained elusive thus far, and importantly, how these obstacles may be overcome. For example, for delta opioid agonists to be effective, a state of inflammation may be required as this induces delta opioid receptors to migrate to the surface of neuronal cells and thereby become accessible to delta opioid agonists. Studies have shown

that delta opioid agonists can provide relief of inflammatory pain and malignant bone pain. Meanwhile, peripherally restricted kappa opioid agonists have been developed to target kappa opioid receptors located on visceral and somatic afferent nerves for relief of inflammatory, visceral, and neuropathic chronic pain. The recently shown efficacy of these analgesics combined with a possible lower abuse potential and side effect burden than mu opioid receptor agonists makes delta and peripherally restricted kappa opioid receptor agonists promising targets for treating pain.

Anticonvulsant drugs for acute and chronic pain.
Wiffen PJ, Collins S, McQuay HJ, Carroll D, Jadad A, Moore RA.
Cochrane Database Syst Rev. 2010 Jan 20;(1):CD001133.

BACKGROUND: Anticonvulsant drugs have been used in the management of pain since the 1960s. The clinical impression is that they are useful for chronic neuropathic pain, especially when the pain is lancinating or burning. Readers are referred to reviews of carbamazepine and gabapentin in T he Cochrane Library which replace the information on those drugs in this review. Other drugs remain unchanged at present in this review OBJECTIVES: To evaluate the analgesic effectiveness and adverse effects of anticonvulsant drugs for pain management in clinical practice . Migraine and headache studies are excluded in this revision. SEARCH STRATEGY: Randomised trials of anticonvulsants in acute, chronic or cancer pain were identified by MEDLINE (1966-1999), EMBASE (1994-1999), SIGLE (1980 to 1999) and the Cochrane Controlled Trials Register (CENTRAL/CCTR) (The Cochrane Library Issue 3, 1999). In addition, 41 medical journals were hand searched. Additional reports were identified from the reference list of the retrieved papers, and by contacting investigators. Date of most recent search: September 1999. SELECTION CRITERIA: Randomised trials reporting the analgesic effects of anticonvulsant drugs in patients, with subjective pain assessment as either the primary or a secondary outcome. DATA COLLECTION AND ANALYSIS: Data were extracted by two independent review authors, and trials were quality scored. Numbers-needed-to-treat (NNTs) were calculated from dichotomous data for effectiveness, adverse effects and drug-related study withdrawal, for individual studies and for pooled data. MAIN RESULTS: Twenty-three trials of six anticonvulsants were considered eligible (1074 patients).The only placebo-controlled study in acute pain found no analgesic effect of sodium valproate.Three placebo-controlled studies of carbamazepine in trigeminal neuralgia had a combined NNT (95% confidence interval (CI)) for effectiveness of 2.5 (CI 2.0 to 3.4). A single placebo-controlled trial of gabapentin in post-herpetic neuralgia had an NNT of 3.2 (CI 2.4 to 5.0). For diabetic neuropathy NNTs for effectiveness were as follows: (one RCT for each drug) carbamazepine 2.3 (CI 1.6 to 3.8), gabapentin 3.8 (CI 2.4 to 8.7) and phenytoin 2.1 (CI 1.5 to 3.6).Numbers-needed-to-harm (NNHs) were calculated where possible by combining studies for each drug entity irrespective of the condition treated. The results were, for minor harm, carbamazepine 3.7 (CI 2.4 to 7.8), gabapentin 2.5 (CI 2.0 to 3.2), phenytoin 3.2 (CI 2.1 to 6.3). NNHs for major harm were not statistically significant for any drug compared with placebo.Phenytoin had no effect in irritable bowel syndrome, and carbamazepine little effect in post-stroke pain. Clonazepam was effective in one study of temporomandibular joint dysfunction. AUTHORS' CONCLUSIONS: Although anticonvulsants are used widely in chronic pain surprisingly few trials show analgesic effectiveness. Only one study identified considered cancer pain. There is no evidence that anticonvulsants are effective for acute pain. In chronic pain syndromes other than trigeminal neuralgia, anticonvulsants should be withheld until other interventions have been tried. While gabapentin is increasingly being used for neuropathic pain the evidence would suggest that it is not superior to carbamazepine.

The endocannabinoid system and pain.
Guindon J, Hohmann AG.
CNS Neurol Disord Drug Targets. 2009 Dec;8(6):403-21.

The therapeutic potential of cannabinoids has been the topic of extensive investigation following the discovery of cannabinoid receptors and their endogenous ligands. Cannabinoid receptors and their endogenous ligands are present at supraspinal, spinal and peripheral levels. Cannabinoids suppress behavioral responses to noxious stimulation and suppress nociceptive processing through activation of

cannabinoid CB(1) and CB(2) receptor subtypes. Endocannabinoids, the brain's own cannabis-like substances, share the same molecular target as Delta(9)-tetrahydrocannabinol, the main psychoactive component in cannabis. Endocannabinoids serve as synaptic circuit breakers and regulate multiple physiological and pathological conditions, e.g. regulation of food intake, immunomodulation, inflammation, analgesia, cancer, addictive behavior, epilepsy and others. This review will focus on uncovering the roles of anandamide and 2-arachidonoylglycerol, the two best characterized endocannabinoids identified to date, in controlling nociceptive responding. The roles of anandamide and 2-arachidonoylglycerol, released under physiological conditions, in modulating nociceptive responding at different levels of the neuraxis will be emphasized in this review. Effects of modulation of endocannabinoid levels through inhibition of endocannabinoid hydrolysis and uptake is also compared with effects of exogenous administration of synthetic endocannabinoids in acute, inflammatory and neuropathic pain models. Finally, the therapeutic potential of the endocannabinoid signaling system is discussed in the context of identifying novel pharmacotherapies for the treatment of pain.

The thalamic nucleus submedius and ventrolateral orbital cortex are involved in nociceptive modulation: a novel pain modulation pathway.
Tang JS, Qu CL, Huo FQ.
Prog Neurobiol. 2009 Dec;89(4):383-9.

Recently, a series of studies have given rise to and provided evidence for the hypothesis that the nucleus submedius (Sm) in the medial thalamus is involved in modulation of nociception. The Sm, ventrolateral orbital cortex (VLO) and the periaqueductal gray (PAG) constitute a pain modulatory pathway, activation of which leads to activation of the PAG-brainstem descending inhibitory system and depression of the nociceptive inputs in the spinal cord and trigeminal nucleus. Other studies have indicated that the Sm-VLO-PAG pathway plays an important role in the analgesia induced by electroacupuncture stimulation of the acupuncture point (acupoint) for exciting small diameter fiber (A-delta and C group) afferents. Opioid peptides, serotonin, dopamine, glutamate and their related receptors are involved in Sm- and/or VLO-mediated descending antinociception, and a GABAergic disinhibitory mechanism participates in mediating the antinociception induced by activation of mu-opioid receptors, serotonin 1(A) receptors, and dopamine D(2)-like receptors. This review describes these findings, which provide important new insights into the roles of the thalamus and cerebral cortex in descending pain modulation.

Critical role of nociceptor plasticity in chronic pain.
Reichling DB, Levine JD.
Trends Neurosci. 2009 Dec;32(12):611-8.
The transition from acute to chronic pain states might be the most important challenge in research to improve clinical treatment of debilitating pain. We describe a recently identified mechanism of neuronal plasticity in primary afferent nociceptive nerve fibers (nociceptors) by which an acute inflammatory insult or environmental stressor can trigger long-lasting hypersensitivity of nociceptors to inflammatory cytokines. This phenomenon, "hyperalgesic priming," depends on the epsilon isoform of protein kinase C (PKCepsilon) and a switch in intracellular signaling pathways that mediate cytokine-induced nociceptor hyperexcitability. We discuss the impact of this discovery on our understanding of, and ultimately our ability to treat, a variety of enigmatic and debilitating pain conditions, including those associated with repetitive injury, and generalized pain conditions, such as fibromyalgia.

Other Vulvovaginal Disorders

Recognizing and treating urogenital atrophy in postmenopausal women.
Goldstein I.
J Womens Health (Larchmt). 2010 Feb 15. [Epub ahead of print]

Abstract Urogenital atrophy resulting from postmenopausal estrogen deficiency has numerous clinical effects, including vaginal dryness, sexual dysfunction, urinary incontinence, and recurrent urinary tract infections (UTIs), all of which can cause significant distress and reduction in quality of life. Although nearly one third to one half of postmenopausal women experience these symptoms, they are often overlooked because patients may be reluctant to discuss them and clinicians fail to screen for them. As these symptoms are unlikely to resolve without treatment, the prompt diagnosis and treatment of urogenital atrophy is essential. Estrogen therapy, administered either locally or systemically, provides significant relief from symptoms related to urogenital atrophy. However, systemic estrogen therapy is contraindicated in some women and may not be accepted in women without other menopausal symptoms. Local low-dose vaginal estrogen therapy, in the form of vaginal estrogen tablets, creams, or rings, has been shown to reduce dyspareunia and vaginal dryness, restore vaginal pH, and restore normal vaginal cytology. All forms of vaginal estrogen therapy are effective and well tolerated, although vaginal tablets and rings may have fewer adverse effects and have higher rates of adherence than creams.

Vulvovaginal atrophy.
Mac Bride MB, Rhodes DJ, Shuster LT.
Mayo Clin Proc. 2010 Jan;85(1):87-94.

Vulvovaginal atrophy (VVA) is a common and underreported condition associated with decreased estrogenization of the vaginal tissue. Symptoms include dryness, irritation, soreness, and dyspareunia with urinary frequency, urgency, and urge incontinence. It can occur at any time in a woman's life cycle, although more commonly in the postmenopausal phase, during which the prevalence is close to 50%. Clinical findings include the presence of pale and dry vulvovaginal mucosa with petechiae. Vaginal rugae disappear, and the cervix may become flush with the vaginal wall. A vaginal pH of 4.6 or more supports the diagnosis of VVA. Even while taking systemic estrogen, 10% to 20% of women may still have residual VVA symptoms. Breast cancer treatment increases the prevalence of VVA because the surgical, endocrine, and chemotherapeutic agents used in its treatment can cause or exacerbate VVA. Local estrogen treatment for this group of women remains controversial.

Ospemifene effectively treats vulvovaginal atrophy in postmenopausal women: results from a pivotal phase 3 study.
Bachmann GA, Komi JO; The Ospemifene Study Group.
Menopause. 2009 Dec 20. [Epub ahead of print]

OBJECTIVE:: The aim of this study was to study the efficacy and safety of ospemifene, a new selective estrogen receptor modulator, in the treatment of vulvovaginal atrophy in postmenopausal women. METHODS:: A randomized, double-blind phase 3 study in which 826 postmenopausal women were randomized 1:1:1 to receive treatment with ospemifene 30 or 60 mg/day or placebo orally for 12 weeks was conducted. The primary inclusion criteria were having 5% or less superficial cells on the vaginal smear (maturation index), vaginal pH greater than 5.0, and at least one moderate or severe symptom of vulvovaginal atrophy. The four coprimary endpoints were the change from baseline to 12 weeks in the percentage of superficial and parabasal cells on the vaginal smear, change in vaginal pH, and change in severity of most bothersome symptom (vaginal dryness or dyspareunia) compared with placebo. All participants were given a nonhormonal vaginal lubricant for use as needed. RESULTS:: Ospemifene was statistically significantly superior to placebo in each of the coprimary endpoints at the 60-mg dose. Statistically significant results were achieved for all coprimary endpoints with the 30-mg dose except for

dyspareunia. Ospemifene was well tolerated at both doses and demonstrated a favorable safety profile. CONCLUSIONS:: Ospemifene was shown to be effective and well tolerated for the treatment of the symptoms of vaginal dryness and dyspareunia associated with vulvovaginal atrophy over and above the use of provided lubricants.

Efficacy and tolerability of local estrogen therapy for urogenital atrophy.
Archer DF.
Menopause. 2010 Jan-Feb;17(1):194-203.

OBJECTIVE: This study aimed to identify vaginal discomfort in the form of dryness, itching, burning, and dyspareunia, which remains an inadequately addressed clinical problem for many postmenopausal women, and to describe the age or menopause-related dysfunction of the female urethral tract, which is prevalent. METHODS: Medical literature on the incidence and treatment of vulvovaginal symptoms in postmenopausal women was reviewed. RESULTS: Urogenital atrophy should not be considered an inevitable consequence of menopause because various hormonal and nonhormonal products are available to relieve symptoms. Estrogen deficiency is the primary cause of atrophic urogenital changes, and postmenopausal estrogen therapy is the most logical choice for treatment. All available low-dose local estrogen formulations are effective, but the optimal dose and preferred mode of estrogen administration to achieve symptom relief can vary from woman to woman. Individualization of therapy is the key to balancing the desired local effects of topical vaginal estrogens with potential systemic effects, which may or may not be desired. CONCLUSIONS: This article reviews the use of products for the management of urogenital atrophy in terms of their efficacy, safety, and other characteristics that may influence prescribing and woman's preference.

Paget disease of the vulva: a study of 56 cases.
Shaco-Levy R, Bean SM, Vollmer RT, Jewell E, Jones EL, Valdes CL, Bentley RC, Selim MA, Robboy SJ.
Eur J Obstet Gynecol Reprod Biol. 2010 Mar;149(1):86-91.

OBJECTIVE: To resolve controversial issues regarding vulvar Paget disease through analysis of a substantial number of cases. STUDY DESIGN: The medical records and pathology slides of 56 patients with a diagnosis of vulvar Paget disease were reviewed. Possible correlation between clinical and pathological data was examined. RESULTS: Most patients were Caucasian and their mean age at diagnosis was 69 years. The average length of follow-up was 5.6 years. The most common symptom was pruritus, almost always accompanied by erythematous-white plaques. Substantial delay between appearance of symptoms and diagnosis was observed in many patients, and was significantly associated with larger lesions. Recurrence rate after surgical management was 32%, with disease involving the perineum being the only statistically significant risk factor. Patients with positive surgical margins had an increased recurrence rate, but this was not statistically significant. Intra-operative frozen section analysis of the margins as well as radical surgery as initial treatment did not reduce recurrence rate. In general, stromal invasion was not associated with worse prognosis, but the single patient who died of disease had the deepest stromal invasion. Radiation therapy given to five patients who either had multiple positive surgical margins or experienced disease recurrence and refused additional surgery resulted in complete response with no further recurrences. On the last day of follow-up 24 patients (43%) had no evidence of disease, 24 patients (43%) were dead of other causes, 5 patients (9%) were alive with disease, 2 patients (3%) were lost to follow-up, and 1 (2%) died due to vulvar Paget disease with invasive adenocarcinoma. CONCLUSIONS: Vulvar Paget disease only rarely results in a patient's death, but long term follow-up is required, as recurrences are common and can be noted many years after the initial treatment.

Chronic vulvar fissure--a rare manifestation of mycosis fungoides.
Reichman O, Sobel JD, Bentley G.
J Low Genit Tract Dis. 2010 Jan;14(1):65-7.

BACKGROUND: Vulvar fissures are a common cause of vulvar pain and discomfort. The differential diagnosis of the underlying process is broad, and some cases remain undiagnosed. Mycosis fungoides, the dominant component of cutaneous T-cell lymphoma, rarely present as fissures. We report a case of a chronic vulvar fissure due to mycosis fungoides. CASE: A 55-year-old woman was referred to the vaginitis clinic for evaluation of a chronic vulvar fissure, 6 cm in length, located at the left interlabial sulcus. A detailed history and examination for other skin lesions revealed an erythematous pruritic patch on left breast that had been present for years. Repeat biopsies from both sites showed a dense dermal lymphocytic infiltrate composed predominantly of CD3- and CD4-positive T cell with minimal epidermotropism. A T-gamma polymerase chain reaction analysis demonstrated a clonal T-cell rearrangement. Based on a diagnostic algorithm that combines clinical features, histopathology, and molecular biology, a diagnosis of mycosis fungoides was confirmed. CONCLUSIONS: Patients presenting with vulvar lesions should always be suspected of having an underlying dermatosis, and a detailed examination for other skin lesions should be performed. In the presented case, once both skin lesions were linked clinically, repeat biopsies of both sites led to a confirmed diagnosis of mycosis fungoides.

High-intensity focused ultrasound treatment for non-neoplastic epithelial disorders of the vulva.
Ruan L, Xie Z, Wang H, Jiang J, Shi H, Xu J.
Int J Gynaecol Obstet. 2010 Feb 12. [Epub ahead of print]

OBJECTIVE: To assess the efficacy of high-intensity focused ultrasound (HIFU) treatment in patients with non-neoplastic epithelial disorders of the vulva. METHOD: We reviewed 41 cases of lichen sclerosus, 38 cases of squamous cell hyperplasia, and 17 mixed cases treated by HIFU from April 2004 to July 2008 at the Women's Hospital of Zhejiang University School of Medicine. Biopsy specimens were assessed with light microscopy before and after treatment. RESULTS: Pruritus and signs of vulvar lesions were dramatically improved following HIFU treatment, without severe complications, and 90.23% of the patients were cured or had their symptoms improved 6months after treatment. On light microscopy, pigmentation and epithelial structures were recovered and dermal lymphocytic infiltration was reduced. The response rates were lower and complication rates higher among lichen sclerosus than among squamous cell hyperplasia cases ($P<0.05$ for both). CONCLUSION: Treatment with HIFU may be safe and effective in cases of vulvar dystrophy.

Lichen sclerosus: role of occlusion of the genital skin in the pathogenesis.
Gupta S, Malhotra AK, Ajith C.
Indian J Dermatol Venereol Leprol. 2010 Jan-Feb;76(1):56-8.

Lichen sclerosus (LS) is a chronic inflammatory skin disease, which most commonly involves the anogenital region. The etiology of LS is obscure, but genetic susceptibility, autoimmune mechanisms, infective agents like human papillomavirus and spirochaetes, and Koebner phenomenon has been postulated as causative factors. We report our observation in 6 patients (3 males and 3 females) with histologically proven lichen sclerosus that showed relative sparing of the uncovered areas of the genitals, thereby suggesting that the occlusion of the genital skin may be playing a greater role in the causation of LS than is currently thought, in both sexes.

Hypoxia-ischaemia is involved in the pathogenesis of vulvar lichen sclerosus.
Li YZ, Wu Y, Zhang QH, Wang Y, Zhen JH, Li SL.
Clin Exp Dermatol. 2009 Dec;34(8):e531-6.

BACKGROUND: Lichen sclerosus (LS) is a chronic inflammatory skin disease, the pathogenesis of which is poorly understood. AIM: To evaluate the role of hypoxia-ischaemia (HI) in vulvar LS. METHODS:

Samples from five patients with vulvar LS and five control subjects were collected for analysis by transmission electron microscopy (TEM) to reveal the ultrastructural changes of organelles and dermal blood capillaries. Samples from 37 patients with vulvar LS and 12 control subjects were collected for immunohistochemistry to detect the expression of vascular endothelial growth factor (VEGF) and the hypoxia markers hypoxia-inducible factor (HIF)-1alpha and glucose transporter (Glut)-1. RESULTS: Using TEM, the mitochondria of basal cells and vascular endothelial cells in vulvar LS tissue were found to be swollen with loss of cristae, and the rough endoplasmic reticulum had luminal swelling and ribosomal detachment. Damage to vascular endothelial cells, disorganization of capillary architecture and loss of capillaries were also seen. By immunohistochemistry, moderate to intense staining of VEGF was seen in almost 90% of control sections vs. about 55% of LS sections. Glut-1 expression was negative or weak in 75% of control sections vs. moderate to very strong in about 80% of vulvar LS sections. Nuclear staining of HIF-1alpha was not found in LS or control tissue. CONCLUSIONS: HI is involved in the pathogenesis of vulvar LS.

Treatment considerations for bacterial vaginosis and the risk of recurrence.
Chen JY, Tian H, Beigi RH.
J Womens Health (Larchmt). 2009 Dec;18(12):1997-2004.

BACKGROUND: Recommended regimens for the treatment of bacterial vaginosis (BV) have similar efficacy; thus, the choice of treatment should consider additional factors such as risk of BV recurrence and side effect profile. The purpose of this study was to investigate BV recurrence rates and rates of acquiring vulvovaginal candidiasis (VVC) after different BV treatments in a commercially insured population. METHODS: Private administrative insurance claims from 2004 to 2006 were used. Study subjects were continuously enrolled females 12-50 years of age who filled prescriptions for BV treatment (n=32,268). The four BV treatments (single-dose clindamycin vaginal cream (2%), multiple-dose clindamycin vaginal regimens, vaginal metronidazole, and oral metronidazole) were compared for rates of recurrent BV and VVC after treatment using multivariate analyses. Covariates included sociodemographic and clinical characteristics. RESULTS: Overall, the rate of BV recurrence (2.7%), and VVC posttreatment (2.9%) were low. Women who were treated with single-dose clindamycin vaginal cream (2%) showed no significant difference from women treated with oral metronidazole in the likelihood of BV recurrence. However, women who received other vaginal treatments were significantly more likely to experience BV recurrence compared with women who received oral metronidazole ($p<0.01$). Moreover, women who were treated with single-dose clindamycin vaginal cream (2%) and vaginal metronidazole were significantly less likely to have VVC compared with those treated with oral metronidazole ($p<0.01$). CONCLUSIONS: This study suggests that single-dose clindamycin vaginal cream (2%) may be a good alternative to oral metronidazole for the treatment of BV, given the low rates of recurrence and subsequent VVC demonstrated in this analysis.

Mannan-binding lectin in women with a history of recurrent vulvovaginal candidiasis.
Henić E, Thiel S, Mårdh PA.
Eur J Obstet Gynecol Reprod Biol. 2010 Feb;148(2):163-5.
OBJECTIVES: To determine the serum concentration of mannan-binding lectin (MBL), a component of the innate immune system, in women with a history of recurrent vulvovaginal candidiasis (RVVC) and to correlate the result to candida-cultures, contraceptive use, if any, and to different antifungal therapies. STUDY DESIGN: Twenty-nine women with a history of RVVC were investigated. Cultures of vulvar and vaginal samples were grown on chromogenic agar. Serum levels of MBL were determined by a sandwich time-resolved immunofluorometric assay, using anti-MBL coated microtiter wells containing samples, which were washed, incubated with biotinylated anti-MBL followed by europium-labeled streptavidin and measured by time-resolved flourometry. RESULTS: The median MBL level was higher in the RVVC cases than in 30 women with no history of genital candida infection who served as a comparison group ($p=0.006$). It was also higher in the candida-positive than in the culture-negative RVVC ($p=0.02$). The median concentration of MBL was also higher in hormonal contraceptive users as compared to condom-users and those using no contraceptive at all ($p=0.03$). CONCLUSION: The result indicates a role of MBL

in RVVC and the production may correlate to vulvar/vaginal colonization by Candida, hormonal contraceptive use, and antifungal therapies.

Vaginal microbiocoenosis and cytology of prepubertal and adolescent girls: their role in health and disease.
Matytsina LA, Greydanus DE, Gurkin YA.
World J Pediatr. 2010 Feb;6(1):32-7.

BACKGROUND: Clinicians and investigators often do not appreciate the importance of vaginal microbiocoenosis and vaginal cytology in the health of prepubertal and adolescent girls. DATA SOURCES: Based on recent publications in human medicine and our own experience with vaginal cytology and microbiology in children and adolescent girls, we review the principles of vaginal microbiocoenosis and cytology and their roles in disease prevention in prepubertal and adolescent girls. RESULTS: The main role of vaginal microbiocoenosis and cytology in diagnosing as well as developing vulvovaginitis is demonstrated. Clinicians can identify states of vaginal health and disease by important well-known diagnostic tools, including vaginal cytology. Lactobacilli are infrequently observed in the prepubertal girls, but become more abundant in adolescent girls. Three basic types of vaginal smears are presented in addition to a classification of inflammatory urogenital diseases. Management of common types of vulvovaginitis is also considered. CONCLUSIONS: This essential shift in vaginal biocoenosis is important to prevent the growth of potentially pathogenic flora in the vagina. The detection of vaginal microbiocoenosis problems and recognition of changing cytology in vaginal development can provide helpful clues to identifying and preventing vaginal diseases in this pediatric population.

Anatomy / Basic Science

Identification of perineal sensory neurons activated by innocuous heat.
Kiasalari Z, Salehi I, Zhong Y, McMahon SB, Michael-Titus AT, Michael GJ.
J Comp Neurol. 2010 Jan 10;518(2):137-62.

C-fiber sensory neurons comprise nociceptors and smaller populations of cells detecting innocuous thermal and light tactile stimuli. Markers identify subpopulations of these cells, aiding our understanding of their physiological roles. The transient receptor potential vanilloid 1 (TRPV1) cation channel is characteristic of polymodal C-fiber nociceptors and is sensitive to noxious heat, irritant vanilloids, and protons. By using immunohistochemistry, in situ hybridization, and retrograde tracing, we anatomically characterize a small subpopulation of C-fiber cells that express high levels of TRPV1 (HE TRPV1 cells). These cells do not express molecular markers normally associated with C-fiber nociceptors. Furthermore, they express a unique complement of neurotrophic factor receptors, namely, the trkC receptor for neurotrophin 3, as well as receptors for neurturin and glial cell line-derived neurotrophic factor. HE TRPV1 cells are distributed in sensory ganglia throughout the neuraxis, with higher numbers noted in the sixth lumbar ganglion. In this ganglion and others of the lumbar and sacral regions, 75% or more of such HE TRPV1 cells express estrogen receptor alpha, suggestive of their regulation by estrogen and a role in afferent sensation related to reproduction. Afferents from these cells provide innervation to the hairy skin of the perineal region and can be activated by thermal stimuli from 38 degrees C, with a maximal response at 42 degrees C, as indicated by induction of extracellular signal-regulated kinase phosphorylation. We hypothesize that apart from participating in normal thermal sensation relevant to thermoregulation and reproductive functions, HE TRPV1 cells may mediate burning pain in chronic pain syndromes with perineal localization.

PI3K modulates estrogen-dependent facilitation of colon-to-urethra cross-organ reflex sensitization in ovariectomized female rats.
Peng HY, Chen GD, Lai CY, Hsieh MC, Hsu HH, Wu HC, Lin TB.
J Neurochem. 2010 Jan 8. [Epub ahead of print]

Abstract To determine the role of 17beta-estradiol and involvement of intracellular phosphatidylinositol-3-kinase signaling in cross-organ sensitization between the descending colon and the urethra, we analyzed urethra reflex activity and protein expressions in lumbosacral (L6-S2) spinal dorsal horn in response to mustard oil instillation into the descending colon in ovariectomized female rats. When compared with vehicle solution, intracolonic mustard oil sensitized the NMDA receptor NR2B subunit-dependent reflex activity and increased expression levels of phosphorylated Akt (pAkt) and phosphorylated NR2B (pNR2B) in dorsal horn. Facilitation of reflex sensitization and increases in protein expressions of pAkt and pNR2B in dorsal horn were induced after pre-treatment with a subcutaneous injection of 17beta-estradiol (5 mug/kg), 6 h ahead of time, when compared with vehicle solution. This phenomenon was reversed both by intrathecal pre-treatment with ICI 182780 (0.25 mg/kg, i.t.) and LY294002 (50 mg/kg, i.t.). Immunoprecipitation of dorsal horn tissue revealed a protein-protein interaction between pAkt and pNR2B increases, 6 h following the subcutaneous 17beta-estradiol when compared with vehicle injections. Results indicate 17beta-estradiol may activate the phosphatidylinositol-3-kinase cascade, which subsequently phosphorylates the NR2B subunit, via spinal estrogen receptors ERalpha/ERbeta, to facilitate NMDA-dependent cross-organ sensitization, which is presumed to underlie pelvic viscero-visceral referred pain.

A unique variation of the pudendal nerve.
Yi SQ, Itoh M.
Clin Anat. 2010 Jan 12. [Epub ahead of print]

No abstract available.

Estrogen receptor-α expression in nociceptive-responsive neurons in the medullary dorsal horn of the female rat.
Amandusson A, Blomqvist A.
Eur J Pain. 2010 Mar;14(3):245-8.

Estrogens exert a substantial influence on the transmission of nociceptive stimuli and the susceptibility to pain disorders as made evident by studies in both animals and human subjects. The estrogen receptor (ER) seems to be of crucial importance to the cellular mechanisms underlying such an influence. However, it has not been clarified whether nociceptive neurons activated by pain express ERs. In this study, a noxious injection of formalin was given into the lower lip of female rats, thereby activating nociceptive neurons in the trigeminal subnucleus caudalis as demonstrated by immunohistochemical labeling of Fos. Using a dual-label immunohistochemistry protocol ERalpha-containing cells were visualized in the same sections. In the superficial layers of the medullary dorsal horn, 12% of ERalpha-labeled cells, mainly located in lamina II, also expressed noxious-induced Fos. These findings show that nociceptive-responsive neurons in the medullary dorsal horn express ERalpha, thus providing a possible morphological basis for the hypothesis that estrogens directly regulate pain transmission at this level.