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This newsletter is quarterly and contains abstracts from medical journals published between September and December 2009. Abstracts presented at scientific meetings may also be included. Please direct any comments regarding this newsletter to chris@nva.org.

Pain

Neuroscience: Unbearable lightness of touch.

Drew LJ, MacDermott AB.
Nature 2009 Dec 3;462(7273):580-1.

Following inflammation or nerve injury, stimuli that are normally perceived as innocuous can evoke persistent pain. A population of neurons that contributes to this syndrome has now been identified.

Injury-induced mechanical hypersensitivity requires C-low threshold mechanoreceptors.

Seal RP, Wang X, Guan Y, Raja SN, Woodbury CJ, Basbaum AI, Edwards RH.
Nature. 2009 Dec 3;462(7273):651-5.

Mechanical pain contributes to the morbidity associated with inflammation and trauma, but primary sensory neurons that convey the sensation of acute and persistent mechanical pain have not been identified. Dorsal root ganglion (DRG) neurons transmit sensory information to the spinal cord using the excitatory transmitter glutamate, a process that depends on glutamate transport into synaptic vesicles for regulated exocytotic release. Here we report that a small subset of cells in the DRG expresses the low abundance vesicular glutamate transporter VGLUT3 (also known as SLC17A8). In the dorsal horn of the spinal cord, these afferents project to lamina I and the innermost layer of lamina II, which has previously been implicated in persistent pain caused by injury. Because the different VGLUT isoforms generally have a non-redundant pattern of expression, we used Vglut3 knockout mice to assess the role of VGLUT3(+) primary afferents in the behavioural response to somatosensory input. The loss of VGLUT3 specifically impairs mechanical pain sensation, and in particular the mechanical hypersensitivity to normally innocuous stimuli that accompanies inflammation, nerve injury and trauma. Direct recording from VGLUT3(+) neurons in the DRG further identifies them as a poorly understood population of unmyelinated, low threshold mechanoreceptors (C-LTMRs). The analysis of Vglut3(-/-) mice now indicates a critical role for C-LTMRs in the mechanical hypersensitivity caused by injury.

Absence of pain with hyperhidrosis: a new syndrome where vascular afferents may mediate cutaneous sensation.

Bowsher D, Geoffrey Woods C, Nicholas AK, Carvalho OM, Haggett CE, Tedman B, Mackenzie JM, Crooks D, Mahmood N, Tworney JA, Hann S, Jones D, Wymer JP, Albrecht PJ, Argoff CE, Rice FL. Pain. 2009 Dec 15;147(1-3):287-98.

Congenital absence of pain perception is a rare phenotype. Here we report two unrelated adult individuals who have a previously unreported neuropathy consisting of congenital absence of pain with hyperhidrosis (CAPH). Both subjects had normal intelligence and productive lives despite failure to experience pain due to broken bones, severe cold or burns. Functional assessments revealed that both are generally hypesthetic with thresholds greater than two standard deviations above normal for a several of modalities in addition to noxious stimuli. Sweating was 3 to 8-fold greater than normal. Sural nerve biopsy showed that all types of myelinated and unmyelinated fibers were severely reduced. Extensive multi-antibody immunofluorescence analyses were conducted on several skin biopsies from the hands and back of one CAPH subject and two normal subjects. The CAPH subject had all normal types of immunochemically and morphologically distinct sensory and autonomic innervation to the vasculature and sweat glands, including a previously unknown cholinergic arterial innervation. Virtually all other types of normal cutaneous C, Adelta and Abeta-fiber endings were absent. This subject had no mutations in the genes SCN9A, SCN10A, SCN11A, NGFB, TRKA, NRTN and GFRA2. Our findings suggest three hypotheses: (1) that development or maintenance of sensory innervation to cutaneous vasculature and sweat glands may be under separate genetic control from that of all other cutaneous sensory innervation, (2) the latter innervation is preferentially vulnerable to some environmental factor, and (3) vascular and sweat gland afferents may contribute to conscious cutaneous perception.

Are we getting anywhere in human pain genetics?

Mogil JS

Pain. 2009 Dec;146(3):231-2.

No abstract available.

Vulvodynia / Vulvovaginal Pain

Allergic reactions and risk of vulvodynia.

Harlow BL, He W, Nguyen RH.

Ann Epidemiol. 2009 Nov;19(11):771-7.

PURPOSE: A recent histological study of vestibular tissue from women with localized vulvodynia found universal presence of mast cells compared to no presence in vestibular tissue among controls. Since histamine is generated by mast cells, and mast cells contribute to the production of cytokines during chronic inflammation, we assessed the association between conditions that elicit a clinically relevant histamine response and vulvodynia. **METHODS:** We studied 239 women with and 239 women without vulvodynia to assess the influence of self-reported allergic reactions antecedent to first development of vulvar pain symptoms among cases, and a matched reference age among controls. **RESULTS:** Women with self-reported hives prior to first report of vulvar pain or reference age among controls were 2.5 times more likely to develop vulvodynia (95% confidence interval [CI], 1.7-4.4). Those reporting a history of allergic reactions to insect bites were 2.1 times more likely (95%CI, 1.1-4.0), and those reporting a history of seasonal allergies were 2.0 times (95%CI, 1.3-3.2) more likely to develop vulvodynia. Findings were similar in a restricted subset of clinically confirmed cases and matched controls. **CONCLUSIONS:** An altered immuno-inflammatory response to environmentally induced allergic reactions may predispose women to the development of vulvodynia or may be markers of an already heightened immuno-inflammatory response.

Gynecological symptoms and sexual behaviors among adolescent women.

Woods JL, Hensel DJ, Fortenberry JD.
J Pediatr Adolesc Gynecol. 2009 Sep 4. [Epub ahead of print]

STUDY OBJECTIVE: The study sought to expand the minimal understanding of the prevalence of gynecological symptoms, such as vulvovaginal pain, pelvic cramps, and vaginal discharge, and the prevalence of the relationship of symptom duration to event-level sexual behaviors. **DESIGN:** Data were daily diaries collected from an ongoing, longitudinal cohort with the three symptom variables **MAIN OUTCOME MEASURES:** Symptom duration was calculated, and event-level sexual behaviors were included. **RESULTS:** It was reported with relative frequency that single symptoms had positive and negative effects, whereas multiple symptoms and long duration of symptoms decreased the likelihood of all noncoital sexual behaviors. **CONCLUSIONS:** Gynecological symptoms influence the likelihood of sexual behaviors, suggesting a complex relationship between the occurrences.

A pilot survey of the impact of menstrual cycles on adolescent health.

Farquhar CM, Roberts H, Okonkwo QL, Stewart AW.
Aust N Z J Obstet Gynaecol. 2009 Oct;49(5):531-6.

BACKGROUND: The experience of menstruation and reproductive health by adolescent girls has been poorly studied in New Zealand. **AIMS:** To develop and pilot a Web-based survey of 16-year-olds' experience of menstruation and reproductive health with the eventual objective of conducting a larger population-based survey. A secondary aim was to report on the experience of menstrual and reproductive health in a group of 16-year-old girls in an urban setting. **METHODS:** A Web-based survey was developed and tested in 2006 with assistance of a multidisciplinary advisory group. The final version of the questionnaire had 146 questions in 11 sections and the topics were menstrual history, general health including use of medications, access to medical care or health information, sexual health, family history and personal information including smoking, height, weight, ethnicity, paid employment of parents, drug and alcohol use and exercise patterns. **RESULTS:** Seventy-five 16-year-old students completed the survey. Twenty-five per cent considered that their periods were quite a bit or a lot of trouble and 10% avoided certain activities during their menstrual periods, nearly 50% of girls always experienced some pain with every period, and 30% had seen a health professional about their period pains. Thirty-three stated that menstruation was moderately to severely painful and that daily activity was affected. Fifty per cent of girls were sexually active and of these 80% described it as painful. **CONCLUSIONS:** The Web-based survey was a successful approach to collecting information and could be used in a larger study.

Persistent pain after caesarean section and vaginal birth: a cohort study.

Kainu JP, Sarvela J, Tiippana E, Halmesmäki E, Korttila KT.
Int J Obstet Anesth. 2009 Sep 2. [Epub ahead of print]

BACKGROUND: Although persistent pain has been described to occur after various types of surgery, little is known about this entity following caesarean section or vaginal birth. We sought to examine the association between mode of delivery and development of persistent pain, as well as the nature and intensity of the pain. **METHODS:** A questionnaire was sent to 600 consecutive Finnish-speaking women within one year of their giving birth. The survey recorded the women's health history, obstetric history, previous pain, details of the caesarean section or vaginal birth, and a description of their pain, if present. **RESULTS:** Persistent pain one year after delivery was significantly more common after caesarean section (42/229, 18%) than after vaginal birth (20/209, 10%; $P=0.011$, OR 2.1 with 95% CI 1.2-3.7). The persistent pain was mild in 55% of the patients in both groups, and intense or unbearable for four caesarean sections and six vaginal births. Persistent pain was significantly more common in women with previous pain ($P=0.013$), previous back pain ($P=0.016$), and any chronic disease ($P=0.016$). The women with persistent pain recalled significantly more pain on the day after caesarean section ($P=0.004$) and vaginal birth ($P=0.001$) than those who did not report persistent pain. **CONCLUSION:** Persistent pain is more common one year after a caesarean section than after vaginal birth. A history of previous pain and pain on the day after delivery correlated with persistent pain.

[Vestibulodynia--the Israeli experience.]

Bornstein J, Zarfati D, Cohen C, Tendler R, Ophir E.
Harefuah. 2009 Jul;148(7):465-70, 474, 473. Article in Hebrew.

The cause of vestibulitis, currently known as vestibulodynia, is still an enigma. Among those attempting to decipher the puzzle, Israeli researchers are well represented. This article reviews the developments in terminology, etiology, treatment, and research directions, with an emphasis on the role of Israeli research. Forty-four articles, covering a range of aspects of vestibulodynia, are testimony to the commendable contribution of Israeli research to the understanding of this disease. For example, the finding of mast cell proliferation and degranulation, enhanced heparanase expression, and the resultant increase and penetration of nerve fibers into the epithelial emanates from Israel. Furthermore, an Israeli first proposed the new name, vestibulodynia. Implemented in the 1980s, immediately after its initiation in the United States, surgical treatment and research in Israel is at the forefront in the world. Israeli teams investigating the effectiveness of surgical treatment conclude that perineoplasty is more successful than any other treatment. Nonetheless, with 57% complete response, and 89% improvement, surgery does not cure all those suffering from vestibulodynia.

Vulvodynia, a step-wise therapeutic prospective cohort study.

Ventolini G, Barhan S, Duke J.
J Obstet Gynaecol. 2009 Oct;29(7):648-50.

Vulvodynia is characterised by the presence of vulval allodynia (pain evoked by non-painful stimuli) and vulval dysaesthesias (burning, soreness, rawness, stinging and irritation). We assessed a protocol for the evaluation and management of vulvodynia. The protocol was based on the most recent evidence available. We began a simple evaluation and proceeded to an aggressive one. From the cohort of 74 patients, 69 patients (93.2%) were adherent to the protocol. A total of 25 patients (36.3%) improved after antibiotic therapy: 14 patients (20.4%) had a positive fungal culture and 11 patients (15.9%) had a positive bacterial culture; none with a positive viral culture. Eight patients (11.6%) improved with dietary modification. Ten patients (14.5%) benefitted from tricyclic medications; 13 patients (18.8%) improved after gabapentin therapy; 13 patients (18.8%) did not show improvement of their condition. Some 56 patients (81.2%) manifested an improvement of their symptoms, which allowed them to achieve painless sexual intercourse

The ACTIV study: Acupuncture treatment in provoked vestibulodynia.

Curran S, Brotto LA, Fisher H, Knudson G, Cohen T.
J Sex Med. 2009 Nov 12. [Epub ahead of print]

ABSTRACT Introduction. Provoked vestibulodynia (PVD) is a distressing genital pain condition affecting 12% of women. Treatment modalities vary and although vestibulectomy has the highest efficacy rates, it is usually not a first-line option. Acupuncture has a long history in the traditional Chinese medicine (TCM) system and operates on the premise that pain results from the blockage or imbalance of important channels. The main principle of treatment is to move Qi and blood to cease genital pain. Aim. To explore effect sizes and feasibility in a pilot study of acupuncture for women with PVD. Methods. Eight women with PVD (mean age 30 years) underwent 10 1-hour acupuncture sessions. Specific placement of the needles depended on the woman's individual TCM diagnosis. TCM practitioners made qualitative notes on participants' feedback after each session. Main Outcome Measures. Self-reported pain (investigator-developed), pain-associated cognitions (Pain Catastrophizing Scale [PCS], Pain Vigilance and Awareness Questionnaire), and sexual response (Female Sexual Function Index) were measured before and after treatment sessions 5 and 10. Qualitative analyses of TCM practitioner notes were performed along with one in-depth case report on the experience of a participant. Results. A repeated measures analysis of variance revealed significant decreases in pain with manual genital stimulation and helplessness on the PCS. An examination of effect sizes also revealed strong (though nonsignificant) effects for improved ability to have intercourse and sexual desire. Qualitative analyses were overall more positive and revealed an improvement in perceived sexual health, reduced pain, and improved mental

well-being in the majority of participants. Conclusions. Effect sizes and qualitative analyses of practitioner-initiated interviews showed overall positive effects of acupuncture, but there were statistically significant improvements only in pain with manual genital stimulation and helplessness. These findings require replication in a larger, controlled trial before any definitive conclusions on the efficacy of acupuncture for PVD can be made.

Prevalence of interstitial cystitis in vulvodynia patients detected by bladder potassium sensitivity.

Kahn BS, Tatro C, Parsons CL, Willems JJ.
J Sex Med. 2009 Oct 20. [Epub ahead of print]

ABSTRACT Introduction. Intravesical potassium sensitivity has been reported in 82% of vulvodynia patients, suggesting the bladder generates their pain and indicating interstitial cystitis (IC)/painful bladder syndrome deserves greater attention in differential diagnosis of vulvodynia. Aims. The aims of this study were to: (i) determine the prevalence of IC as detected by intravesical potassium sensitivity; and (ii) survey for urinary, pelvic pain, and sexually associated symptoms in patients with vulvodynia. Methods. Consecutive patients with vulvodynia were surveyed for urinary and pelvic pain symptoms using the pelvic pain and urgency/frequency (PUF) questionnaire, and tested for abnormal epithelial permeability using the potassium sensitivity test (PST). Rates of positive PST were determined overall and by PUF score range, and were compared in patients with intermittent vs. constant vulvodynia symptoms. Main Outcome Measures. Results of intravesical PST. Results. Of 122 vulvodynia patients, 102 (84%) had a positive PST and 97 (80%) had urologic symptoms. Of the 87 sexually active patients, 81 (93%) reported pain associated with sex. Patients with constant (72/87, 83%) vs. intermittent symptoms (30/35, 86%) had no significant difference in rates of positive PST. Mean PUF score was 13.2. PUF scores of 3-4 were associated with an 86% rate of positive PST; scores 5-9, 44%; 10-14, 84%; 15-19, 87%; 20-24, 86%; and 25 and above, 100%. Conclusion. Most patients with vulvodynia have a positive PST and urgency/frequency, indicating pain of bladder origin (IC). IC deserves far greater consideration in the differential diagnosis of patients with vulvodynia. This represents a dramatic change for the gynecologic paradigm of vulvodynia, which in many cases appears to be referred pain from the urinary bladder. Kahn BS, Tatro C, Parsons CL, and Willems JJ. Prevalence of interstitial cystitis in vulvodynia patients detected by bladder potassium sensitivity.

Evidence for overlap between urological and nonurological unexplained clinical conditions.

Rodríguez MA, Afari N, Buchwald DS; National Institute of Diabetes and Digestive and Kidney Diseases Working Group on Urological Chronic Pelvic Pain.
J Urol. 2009 Nov;182(5):2123-31. Epub 2009 Sep 16. Review.

PURPOSE: Unexplained clinical conditions share common features such as pain, fatigue, disability out of proportion to physical examination findings, inconsistent laboratory abnormalities, and an association with stress and psychosocial factors. We examined the extent of the overlap among urological and nonurological unexplained clinical conditions characterized by pain. We describe the limitations of previous research and suggest several possible explanatory models. **MATERIALS AND METHODS:** Using hallmark symptoms and syndromes as search terms a search of 12 databases identified a total of 1,037 full-length published articles in 8 languages from 1966 to April 2008. The search focused on the overlap of chronic pelvic pain, interstitial cystitis, painful bladder syndrome, chronic prostatitis/chronic pelvic pain syndrome or vulvodynia with fibromyalgia, chronic fatigue syndrome, temporomandibular joint and muscle disorders or irritable bowel syndrome. We abstracted information on authorship, type of case and control groups, eligibility criteria, case definitions, study methods and major findings. **RESULTS:** The literature suggests considerable comorbidity between urological and nonurological unexplained clinical conditions. The most robust evidence for overlap was for irritable bowel syndrome and urological unexplained syndromes with some estimates of up to 79% comorbidity between chronic pelvic pain and symptoms of irritable bowel syndrome. However, most studies were limited by methodological problems, such as varying case definitions and selection of controls. **CONCLUSIONS:** The overlap between urological and selected nonurological unexplained clinical conditions is substantial. Future research should focus on using standardized definitions, and rigorously designed, well controlled studies to further

assess comorbidity, clarify the magnitude of the association and examine common pathophysiological mechanisms.

Pelvic floor hypertonic disorders: identification and management.

Butrick CW.

Obstet Gynecol Clin North Am. 2009 Sep;36(3):707-22.

Patients with hypertonic pelvic floor disorders can present with pelvic pain or dysfunction. Each of the various syndromes will be discussed including elimination disorders, bladder pain syndrome/interstitial cystitis (BPS/IC), vulvodynia, vaginismus, and chronic pelvic pain. The symptoms and objective findings on physical examination and various diagnostic studies will be reviewed. Therapeutic options including physical therapy, pharmacologic management, and trigger point injections, as well as botulinum toxin injections will be reviewed in detail.

Chronic pelvic pain syndromes: clinical, urodynamic, and urothelial observations.

Butrick CW, Sanford D, Hou Q, Mahnken JD.

Int Urogynecol J Pelvic Floor Dysfunct. 2009 Sep;20(9):1047-53.

INTRODUCTION/METHODS: A cohort of 408 patients with bladder pain syndrome/interstitial cystitis (BPS/IC) was evaluated, and findings were discussed in this retrospective chart review. **RESULTS:** Based on the chief complaints, they were divided into four subgroups: BPS/IC (n = 157), CPP (n = 98), vulvodynia/dyspareunia (n = 40), and "other" (n = 113). Similar findings were found in all four subgroups: complaints of voiding dysfunction (70%), dyspareunia (54%), mean PUF score of 15.9 +/- 6.4, and a positive potassium sensitivity test in 83%. Urodynamics revealed a maximal urethral pressure of 131 cm of water and an abnormal uroflow in 80%. Urothelial therapy in the form of intravesical therapeutic anesthetic cocktails provided benefit in all groups (50%, 67%, 73%, and 77% for vulvodynia, CPP, BPS/IC, "other"). **CONCLUSIONS:** All subgroups had similar findings and response to therapy. Five to 10% of patients with chief complaints of stress or urge incontinence or prolapse were also found to have BPS/IC.

EAU guidelines on chronic pelvic pain.

Fall M, Baranowski AP, Elneil S, Engeler D, Hughes J, Messelink EJ, Oberpenning F, de C Williams AC. Eur Urol. 2009 Aug 31. [Epub ahead of print]

CONTEXT: These guidelines were prepared on behalf of the European Association of Urology (EAU) to help urologists assess the evidence-based management of chronic pelvic pain (CPP) and to incorporate the recommendations into their clinical practice. **OBJECTIVE:** To revise guidelines for the diagnosis, therapy, and follow-up of CPP patients. **EVIDENCE ACQUISITION:** Guidelines were compiled by a working group and based on a systematic review of current literature using the PubMed database, with important papers reviewed for the 2003 EAU guidelines as a background. A panel of experts weighted the references. **EVIDENCE SYNTHESIS:** The full text of the guidelines is available through the EAU Central Office and the EAU Web site (www.uroweb.org). This article is a short version of the full guidelines text and summarises the main conclusions from the guidelines on the management of CPP. **CONCLUSIONS:** A guidelines text is presented including chapters on chronic prostate pain and bladder pain syndromes, urethral pain, scrotal pain, pelvic pain in gynaecologic practice, neurogenic dysfunctions, the role of the pelvic floor and pudendal nerve, psychological factors, general treatment of CPP, nerve blocks, and neuromodulation. These guidelines have been drawn up to provide support in the management of the large and difficult group of patients suffering from CPP.

Musculoskeletal pain and sexual function in women.

Rosenbaum TY.

J Sex Med. 2009 Sep 14. [Epub ahead of print]

Introduction. Sexual pain disorders refer to conditions of genital pain that interfere with intercourse. They often have a musculoskeletal component related to the pelvic floor and are included in the DSM-IV as sexual dysfunctions. Musculoskeletal pain (MP) that is not essentially genitally based often interferes with sex as well yet is not considered a distinct sexual dysfunction. MP is generally addressed by psychiatrists, orthopedists, and rheumatologists who are not traditionally trained in sexual medicine, and therefore, the sexual concerns of women with MP often go unaddressed. Aim. The purposes of this review article were to describe how MP is perceived in the literature as affecting sexual function, illustrate how specific MP conditions prevalent in women may affect sexual function, and offer recommendations for clinical practice. Methods. PubMed and Medline searches were performed using the keywords "musculoskeletal pain and sex," "lower back pain and sex," "arthritis and sex," and "fibromyalgia and sex". Main Outcome Measure. Review of the peer-reviewed literature. Results. Most studies cite fatigue, medication, and relationship adjustment as affecting sexuality much as chronic illness does. While musculoskeletal contributors to genital sexual response and pain are considered relevant to sexual function, little is understood about how MP syndromes specifically affect sexual activity. Conclusion. Lack of mobility and MP can restrict intercourse and limit sexual activity, and gender differences are noted in response to pain. Sexual and relationship counseling should be offered as a component of rehabilitative treatment. Physical therapists are uniquely qualified to provide treatment to address functional activities of daily living, including sexual intercourse, and offer advice for modifications in positioning.

Provoked vestibulodynia: Psychological predictors of topical and cognitive-behavioral treatment outcome.

Desrochers G, Bergeron S, Khalifé S, Dupuis MJ, Jodoin M.

Behav Res Ther. 2009 Oct 7. [Epub ahead of print]

Psychological factors have been found to impact the pain experience and associated sexual impairment of women suffering from provoked vestibulodynia (PV). Despite a lack of randomized treatment outcome studies, particularly concerning psychological predictors of outcome, recent studies have shown that topical applications and cognitive-behavioral therapy (CBT) are among the most popular first-line interventions for PV. The present study aimed to determine the extent to which baseline fear-avoidance variables and pain self-efficacy were differentially associated with topical application and CBT outcomes at six-month follow-up. Data were obtained from 97 women who completed a randomized trial comparing these two treatments. Regression analyses revealed that for topical treatment, higher levels of baseline avoidance predicted worse pain and sexual functioning outcomes, whereas higher levels of pain self-efficacy predicted better outcomes. For CBT, higher levels of baseline fear of pain and catastrophizing contributed to higher pain intensity at follow-up, whereas higher levels of pain self-efficacy were associated with less pain. Psychological factors did not predict sexual functioning outcomes for CBT. Consistent with biopsychosocial models of pain and sexual dysfunction, results indicate that psychological factors contribute to pain and sexual impairment following treatment for PV. Specifically, findings suggest that fear-avoidance variables and pain self-efficacy are significant predictors of topical and CBT treatment outcomes in women with PV.

Dyspareunia: a complex problem requiring a selective approach.

Walid MS, Heaton RL.

Sex Health. 2009 Sep;6(3):250-3.

Dyspareunia frequently has a multifactorial aetiology. The problem with the term is that it is not specific enough and does not allow for proper discussion of the very important problem of pain with sexual intercourse, a problem that can be very disturbing to a couple's relationship. We present two cases of patients who had multiple potential anatomic reasons for dyspareunia. The clinical picture, treatment

strategy and the complex nature of deep penetration pain was discussed. We also proposed a new way of defining dyspareunia to allow a more adequate way of studying and discussing the problem.

The DSM diagnostic criteria for dyspareunia.

Binik YM.

Arch Sex Behav. 2009 Oct 15. [Epub ahead of print]

The DSM-IV-TR attempted to create a unitary category of dyspareunia based on the criterion of genital pain that interfered with sexual intercourse. This classificatory emphasis of interference with intercourse is reviewed and evaluated from both theoretical and empirical points of view. Neither of these points of view was found to support the notion of dyspareunia as a unitary disorder or its inclusion in the DSM-V as a sexual dysfunction. It seems highly likely that there are different syndromes of dyspareunia and that what is currently termed "superficial dyspareunia" cannot be differentiated reliably from vaginismus. It is proposed that the diagnoses of vaginismus and dyspareunia be collapsed into a single diagnostic entity called genito-pelvic pain/penetration disorder. This diagnostic category is defined according to five dimensions: percentage success of vaginal penetration; pain with vaginal penetration; fear of vaginal penetration or of genito-pelvic pain during vaginal penetration; pelvic floor muscle dysfunction; medical co-morbidity.

The DSM diagnostic criteria for vaginismus.

Binik YM.

Arch Sex Behav. 2009 Oct 23. [Epub ahead of print]

Vaginal spasm has been considered the defining diagnostic characteristic of vaginismus for approximately 150 years. This remarkable consensus, based primarily on expert clinical opinion, is preserved in the DSM-IV-TR. The available empirical research, however, does not support this definition nor does it support the validity of the DSM-IV-TR distinction between vaginismus and dyspareunia. The small body of research concerning other possible ways or methods of diagnosing vaginismus is critically reviewed. Based on this review, it is proposed that the diagnoses of vaginismus and dyspareunia be collapsed into a single diagnostic entity called "genito-pelvic pain/penetration disorder." This diagnostic category is defined according to the following five dimensions: percentage success of vaginal penetration; pain with vaginal penetration; fear of vaginal penetration or of genito-pelvic pain during vaginal penetration; pelvic floor muscle dysfunction; medical co-morbidity.

[Spinal cord stimulation at the level of the conus medullaris : Treatment option for therapy-resistant postoperative neuralgia of the pudendal nerve.]

Reichart R, Kuhn SA, Vogel I, Walter J, Kalff R.

Schmerz. 2009 Oct 17. [Epub ahead of print] German.

Injuries of the pudendal nerve, due to a perineal tear during delivery for example, can cause significant and debilitating neurological deficits. Aconuresis and anal incontinence, as well as sensory loss of the outer genitals or even impotency in men are the well known consequences. In addition some patients suffer from a severe neuropathic pain syndrome which is resistant to conservative treatment options. Epidural spinal cord stimulation at the level of the terminal cone of the spinal cord may be a new and successful therapeutic concept in otherwise untreatable cases.

[Somatic perineal pain other than pudendal neuralgia.]

Robert R, Labat JJ, Riant T, Louppe JM, Lucas O, Hamel O.
Neurochirurgie. 2009 Oct;55(4-5):470-4. French.

In addition to the well-established syndrome of pudendal compression, and given the rich nerve trunk innervation of the perineum, pain originating in other nerve trunks can occur and must be remembered. Nerves originating high in the thoracolumbar area (ilioinguinal nerve, iliohypogastric nerve, genitor femoral nerve) can be the seat of traumatic lesions occurring during surgical approaches through the abdominal wall or can undergo compressions when crossing the fascia of the large abdominal muscles. Misleading perineal irradiations do not resemble pudendal neuralgia and should suggest pain in these trunks whose cutaneous territories are not solely perineal and whose clinical expression as pain is does not occur in the seated position. Similarly, painful minor intervertebral dysfunction of the thoracolumbar junction is not simply in the mind and should be considered, searched for, and treated. Related more to pudendal neuralgia, pain in the inferior cluneal nerve, triggered by the seated position, should be considered when the pain reaches the lateral anal region, the scrotum, or the labia majora but not involving the glans penis or the clitoris. Specific treatments (physical therapy, infiltrations, surgery) have proven effective.

[The pudendal nerve: clinical and therapeutic morphogenesis, anatomy, and physiopathology.]

Robert R, Labat JJ, Riant T, Louppe JM, Hamel O.
Neurochirurgie. 2009 Oct;55(4-5):463-9. French.

The pudendal is the king of the perineum. Most often originating in the S3 root, it is responsible for the teguments of the perineum (glans penis, clitoris, scrotum, and the labia majora, the skin of the central fibrous perineal body, anus), but also the erector muscles and the striated sphincters. The social nerve, it controls erection and the voluntary sphincters. It is also the nerve of the beginnings of sexual sensation and masturbation. Its injury is expressed in perineal pain, which, when positional, suggests a tunnel syndrome. The compression points have become well known: ligament pinching between the sacrotuberous and sacrospinous ligaments, the falciform process and the pudendal canal (Alcock canal). The data from questioning the patient, the results of the neurological exam, and the at least momentary response to infiltration define the Nantes criteria, which confirm the diagnosis. Treatment is medical, physical therapy, infiltration, and, as a last resort, surgery. The results have improved because of new technical norms, with 75% of operated patients benefiting from surgery. This disorder has become well known and should be remembered, thus sparing the patient from years of suffering and needless consultations for patients who do not present with organ disease, too often implicated instead of a true canal neuropathy, whose clinical manifestation and treatment have now been validated.

Other Vulvovaginal Disorders

[How to diagnose and how to treat diseases of the genital mucosa?]

Parent D.
Rev Med Brux. 2009 Sep;30(4):385-91. French.

The genital area in women is covered by a keratinized squamous stratified epithelium outside the body (vulva), and a non keratinized epithelium inside the body (vagina). These characteristics can have an effect on the clinical aspects of the diseases and/or on the choice of the treatment. Symptoms (itching, pain, vaginal discharge), preferential localisation of skin diseases (psoriasis, lichen planus, lichen sclerosus, atopic dermatitis and allergic contact dermatitis, irritative dermatitis) and the aspect of primary lesions are to be investigated. The implication of this region in sexual activity places it at risk of sexually transmitted diseases (STD's) and dyspareunia. These have numerous causes that have to be sought and taken care of, often by multidisciplinary teams. After a careful history and clinical examination, additional

tests allow to exclude infections or confirm a skin condition or neoplasia by a skin biopsy. If contact dermatitis is suspected, specific allergy testing is done. Treatment starts with correction of harmful habits (excessive use of soaps, inappropriate cosmetic products,...) that add to the local irritation. Patients are then reassured of common misconception regarding cancer, STD's and fertility. In the vast majority of cases, the treatment will target an infection (fungal, bacterial, STD's), will relieve irritation by the use of local immunosuppressant drugs (local corticosteroids) and/or relief itching symptoms with anti-histamine drugs.

Genitourinary manifestations of epstein-barr virus infections.

Leigh R, Nyirjesy P.

Curr Infect Dis Rep. 2009 Nov;11(6):449-56.

Epstein-Barr virus (EBV) is best known as the organism responsible for the syndrome of acute infectious mononucleosis. Transmission of EBV most commonly occurs through oral secretions. EBV has also been isolated from the female genital tract, where its role is poorly understood. This article reviews the available literature and data regarding EBV in the female genital tract and discusses areas of consensus and controversy. The primary manifestation of EBV seems to be vulvar ulcers, which are underrecognized. Diagnosis relies on appropriate serologic testing. Management includes local care and may require pain and corticosteroid medications. Although EBV is present elsewhere in the female genital tract, its pathogenic role in the cervix, uterus, fallopian tubes, and ovaries is poorly understood.

Crohn's disease of the vulva.

Michele AS, Kumaran R, Huyen DH, Giampiero G, Pasquale G.

Int J Surg. 2009 Oct 1. [Epub ahead of print]

Crohn's involvement of the Vulva is unfamiliar and difficult to treat. The aim is to review the presentation, clinical course and different treatments of Vulva Crohn's disease (CD). We have reviewed the literature without language barrier from 1966 to 2009 through Pubmed with the following words: vulva and CD, vulvitis and CD, genital CD. We included articles that had Crohn's involvement of the vulva arising from a distant site (metastatic) or arising from a Crohn's fistula from the perineum and/or anorectum. We excluded CD of other gynaecological organs. One hundred thirty six abstracts were identified and related articles reviewed. Fifty-five cases of CD of the vulva were included in the final analysis of this review. Vulva involvement is rare and gives long-term discomfort. A combined medical therapy (metronidazole with prednisolone) appears to be the most effective treatment. The surgical approach should be reserved for non-responding cases. CD is often unrecognized cause of vulva pain and difficult to diagnose. However if diagnosed and adequately treated it usually responds to conservative therapies.

Urogenital atrophy in breast cancer survivors.

Lester JL, Bernhard LA.

Oncol Nurs Forum. 2009 Nov;36(6):693-8.

PURPOSE/OBJECTIVES: To review the symptoms of urogenital atrophy in breast cancer survivors, influencing factors, and their effects on performance. **DATA SOURCES:** Review of qualitative and quantitative research data that describe pain, function, satisfaction, and quality of life related to urologic, genital, and sexual function. **DATA SYNTHESIS:** Breast cancer treatment can induce or exacerbate symptoms related to urogenital atrophy. The lower urinary and genital tracts are affected by physiologic alterations, the potential abrupt onset of menopause, and treatment side effects. Symptoms of urogenital atrophy often are more prevalent and severe in women treated for breast cancer than in age-matched women without breast cancer. **CONCLUSIONS:** Symptoms related to urogenital atrophy are common in breast cancer survivors and can be affected by physiologic, situational, and psychological influences with negative effects on performance. Research is essential to the understanding of how transient or permanent hormonal alterations affect the urogenital system and the role of these symptoms on quality of life. **IMPLICATIONS FOR NURSING:** Nurses must listen with sensitivity to breast cancer survivors and

their descriptions of these significant and life-altering symptoms. Personalized discussion enables the nurse to explore issues, assess symptoms, recommend interventions, and evaluate at follow-up visits. Nurses are integral to the provision of survivorship care planning that can address the short- and long-term effects of a cancer diagnosis and related treatments.

Efficient diagnosis of vulvovaginal candidiasis using a new rapid immunochromatography test.

Marot-Leblond A, Nail-Billaud S, Pilon F, Beucher B, Poulain D, Robert R.
J Clin Microbiol. 2009 Sep 30. [Epub ahead of print]

Clinical symptoms of vulvovaginal candidiasis (VVC) are non-specific and misdiagnosis is common, leading to a delay in initiation of antifungal treatment. We evaluated a new immunochromatography test (ICT), CandiVagi(R) (SR2B, Avrille, France), for the rapid diagnosis of VVC. This test, which employs an IgM monoclonal antibody to beta-1,2-mannopyranosyl epitopes found in the yeast cell wall, was compared with direct microscopic examination and culture of vaginal swabs. Two-hundred and five women were investigated, including 130 women with symptomatic vaginitis and 75 asymptomatic controls. Two vaginal swabs were obtained from each woman: one was used to prepare wet mount and Gram-stained preparations for direct microscopic examination and was also cultured on Sabouraud dextrose agar for the isolation of *Candida* spp., and the second swab was used for the ICT. The sensitivities of microscopic examination, culture and ICT for the diagnosis of VVC were 61%, 100% and 96.6%, respectively, while the specificities of the three methods were 100%, 82% and 98.6%. The ICT had a negative predictive value of 98.6%, positive predictive value of 96.6% and efficiency of 98%. The ICT provided a rapid result and a better compromise between sensitivity and specificity than conventional microscopy and culture for the diagnosis of VVC. This easy to perform diagnostic test will be useful to practitioners treating women with symptoms of vaginitis.

Targeting the vaginal microbiota with probiotics as a means to counteract infections.

Reid G, Dols J, Miller W.
Curr Opin Clin Nutr Metab Care. 2009 Nov;12(6):583-7.

PURPOSE OF REVIEW: The microbial composition of the vagina of healthy and infected women is becoming more fully elucidated with molecular techniques. The purpose of this review is to examine our current understanding of the vaginal microbiota and assess how probiotic bacteria might reduce infectivity. **RECENT FINDINGS:** It appears that there are some remarkable similarities in the bacterial species that inhabit the vagina of women from diverse ethnic backgrounds. Yet, distinct outliers exist in which a small portion of apparently healthy women have extremely complex microbiota, whereas most have a relatively simple microbiota. Bacterial vaginosis is the most common aberrant condition in women, yet its pathogenesis is poorly understood and it is often asymptomatic. Vulvovaginal candidiasis is better known, yet many women self-treat with antifungals when in fact they have bacterial vaginosis. Urinary tract infection (UTI) remains extremely common, with no real breakthrough treatment or prevention strategy developed in the past 30 or more years. The ability of lactobacilli probiotic interventions to prevent, treat and improve the cure of these infections has long been considered and is now supported by some clinical evidence. **SUMMARY:** The mechanisms whereby certain probiotic lactobacilli improve urogenital health include immune modulation, pathogen displacement and creation of a niche less conducive to proliferation of pathogens and their virulence factors. Probiotics offer a potential new means to prevent urogenital infections and help maintain a healthy vaginal ecosystem.

Effect of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 on the ability of *Candida albicans* to infect cells and induce inflammation.

Martinez RC, Seney SL, Summers KL, Nomizo A, De Martinis EC, Reid G.
Microbiol Immunol. 2009 Sep;53(9):487-95.

Vulvovaginal candidiasis, a high prevailing infection worldwide, is mainly caused by *Candida albicans*. Probiotic *Lactobacillus reuteri* RC-14 and *Lactobacillus rhamnosus* GR-1 have been previously shown to be useful as adjuvants in the treatment of women with VVC. In order to demonstrate and better understand the anti-*Candida* activity of the probiotic microorganisms in an in vitro model simulating vaginal candidiasis, a human vaginal epithelial cell line (VK2/E6E7) was infected with *C. albicans* 3153a and then challenged with probiotic *L. rhamnosus* GR-1 and/or *L. reuteri* RC-14 or their respective CFS (alone or in combination). At each time point (0, 6, 12 and 24 hr), numbers of yeast, lactobacilli and viable VK2/E6E7 cells were determined and, at 0, 6 and 12 hr, the supernatants were measured for cytokine levels. We found that *C. albicans* induced a significant increase in IL-1alpha and IL-8 production by VK2/E6E7 cells. After lactobacilli challenge, epithelial cells did not alter IL-6, IL-1alpha, RANTES and VEGF levels. However, CFS from the probiotic microorganisms up-regulated IL-8 and IP-10 levels secreted by VK2/E6E7 cells infected with *C. albicans*. At 24 hr of co-incubation, *L. reuteri* RC-14 alone and in combination with *L. rhamnosus* GR-1 decreased the yeast population recoverable from the cells. In conclusion, *L. reuteri* RC-14 alone and together with *L. rhamnosus* GR-1 have the potential to inhibit the yeast growth and their CFS may up-regulate IL-8 and IP-10 secretion by VK2/E6E7 cells, which could possibly have played an important role in helping to clear VVC in vivo.

Rapid detection of vaginal *Candida* species by newly developed immunochromatography.

Matsui H, Hanaki H, Takahashi K, Yokoyama A, Nakae T, Sunakawa K, Omura S.
Clin Vaccine Immunol. 2009 Sep;16(9):1366-8.

For the diagnosis of vulvovaginal candidiasis, we developed a simple immunochromatographic method that enables the detection of vaginal *Candida* spp. within about 30 min. Overall, the sensitivity, specificity, positive predictive value, and negative predictive value of this method appeared to be 80.3, 99.3, 98.0, and 92.0%, respectively.

Vulvovaginitis in childhood.

Dei M, Di Maggio F, Di Paolo G, Bruni V.
Best Pract Res Clin Obstet Gynaecol. 2009 Oct 31.

Symptoms related to vulvitis and vulvovaginitis are a frequent complaint in the paediatric age. Knowledge of the risk factors and the pathogenetic mechanisms, combined with thorough clinical examination, helps to distinguish between dermatological diseases, non-specific vulvitis and vulvovaginitis proper. On the basis of microbiological data, the most common pathogens prove to be *Streptococcus pyogenes*, *Haemophilus influenzae* and *Enterobius vermicularis*; fungal and viral infections are less frequent. The possibility of isolating opportunistic pathogens should also be considered. In rare situations, the isolation of a micro-organism normally transmitted by sexual contact should prompt a careful evaluation of possible sexual abuse. Current treatments for specific and non-specific forms are outlined, together with pointers for the evaluation of recurrence.

Use of the VS-sense swab in diagnosing vulvovaginitis.

Sobel JD, Nyirjesy P, Kessary H, Ferris DG.
J Womens Health (Larchmt). 2009 Sep;18(9):1467-70.

BACKGROUND: Although pH assessment of vaginal secretions is beneficial for diagnosing vaginitis, it is not commonly done. The purpose of this study was to determine the performance characteristics of the VS-Sense (pH test) swab (Common Sense, Ltd., Caesarea, Israel) in augmenting the diagnosis of vaginitis. **METHODS:** We prospectively studied 193 women with acute vulvovaginal symptoms and 74

asymptomatic controls at three medical centers. The VS-Sense swab was administered intravaginally, and results were interpreted by a nurse. These results were compared with final clinical and laboratory diagnoses. **RESULTS:** In women with an elevated pH caused by bacterial vaginosis (BV), trichomonas, and other types of vaginitis, the VS-Sense test sensitivity and specificity were 82.3% (102 of 124) (95% CI 74.4%-88.5%) and 94.2% (129 of 137) (95% CI 88.8%-97.4%), respectively. There was an 86.2% (95% CI 81.3%-90.1%) overall agreement between pH paper and VS-Sense swab results. **CONCLUSIONS:** The VS-Sense test offers an alternative approach to measuring vaginal pH with nitrazine paper. Use of this simple, more rapid test may facilitate the diagnosis of vulvovaginitis.

MRSA infection of buttocks, vulva, and genital tract in women.

Reichman O, Sobel JD.

Curr Infect Dis Rep. 2009 Nov;11(6):465-70.

Staphylococcus aureus, although a common commensal bacterium, is a frequent cause of skin and soft tissue infections as well as life-threatening blood stream infections. Resistance to methicillin, which previously was associated with only hospitalized patients, has become a common community-based phenomenon. Less well known is *S. aureus* vaginal colonization and heterosexual transmission, mainly by skin-mucosa contact. Recognizing the vagina as a reservoir is important and should not be ignored, particularly in women presenting with recurrent genital and buttock boils or if their sexual partner has such infections. Vaginal cultures should be obtained from such women; if the vagina is found to be colonized, eradication of *S. aureus* from the vagina should be attempted to reduce infection recurrence.

Sexual functions and depressive symptoms after photodynamic therapy for vulvar lichen sclerosus in postmenopausal women from the upper silesian region of Poland.

Skrzypulec V, Olejek A, Drosdzol A, Nowosielski K, Kozak-Darmas I, Wloch S.

J Sex Med. 2009 Sep 29. [Epub ahead of print]

Introduction. Although lichen sclerosus (LS) may affect women's physical functioning, mood, and quality of life, restricting their physical activities, sexual, and non-sexual contacts, there are limited data on the sexual functioning of women diagnosed with LS. **Aims.** The aim of the study was to evaluate the influence of photodynamic therapy for vulvar LS on sexual functions and depressive symptoms in postmenopausal women from the Upper Silesian Region of Poland. **Methods.** A total of 65 women aged 50-70 visiting an outpatient clinic for assessment of vulvar dermatoses were screened for the clinical trial. Finally, 37 women who met all the inclusion/exclusion criteria were included in the study. All the subjects were treated by topical laser therapy (photodynamic therapy). Sexual functions and depressive symptoms were assessed before and after the therapy using Female Sexual Function Index and Beck Depression Inventory, respectively. **Main Outcome Measures.** Sexual behaviors, sexual functions, and depressive symptoms in females after photodynamic therapy for vulvar LS. **Results.** The total FSFI score was significantly lower after the treatment of vulvar LS as compared with the baseline (median 24.6 vs. 15.9). However, the prevalence of clinically significant FSD was stable throughout the medical intervention except lubrication disorders (higher prevalence after the treatment: 40% vs. 68.57%). Although the scores of BDI at the baseline dropped significantly after the photodynamic therapy (median 12.0 and 9.0, respectively), there were no significant differences in the prevalence of depressive symptoms (48.65% vs. 45.94%). **Conclusions.** Topical laser therapy for vulvar LS has a good clinical outcome, especially in the context of no major negative effects on sexual functioning and the positive impact on the severity of depressive symptoms in postmenopausal women. However, patients should be informed about the possible lubrication disorders following the treatment.

The effect of topical pimecrolimus on inflammatory infiltrate in vulvar lichen sclerosus.

Kauppila S, Kotila V, Knuuti E, Väre PO, Vittaniemi P, Nissi R.
Am J Obstet Gynecol. 2009 Nov 2. [Epub ahead of print]

OBJECTIVE: Lichen sclerosus (LS) is a relatively common chronic inflammatory disorder of the skin and mucosal surfaces. **STUDY DESIGN:** A total of 29 women with histologically confirmed, active LS were recruited to this study with 2 aims. First, we evaluated the effectiveness of pimecrolimus treatment to LS not responding to conventional corticosteroid treatment. The second aim in this study was to provide information of in vivo effects of topical pimecrolimus in acute LS lesions, especially the inflammatory cell infiltration. **RESULTS:** In all, 25 of 29 women applied cream as recommended. After 2 months of treatment, 20 patients had reached partial or complete clinical remission. Histology showed decreased inflammatory lymphoid infiltrate with down-regulation of CD3(+) T cells, CD8(+) T cells, and CD57(+) natural killer cells. Also macrophage marker CD68 staining showed down-regulation. There was no change in CD20(+) B lymphocytes. **CONCLUSION:** We conclude that calcineurin inhibitors are an effective treatment for patients not responding to corticosteroid treatment.

Significant upregulation of antimicrobial peptides and proteins in lichen sclerosus.

Gambichler T, Skrygan M, Tigges C, Kobus S, Gläser R, Kreuter A.
Br J Dermatol. 2009 Nov;161(5):1136-42.

BACKGROUND: Lichen sclerosus (LS) is a chronic inflammatory T cell-driven sclerotic skin condition in which skin barrier disruption frequently occurs. Inflamed and injured epithelia are a particularly rich source of antimicrobial peptides and proteins (AMPs). **OBJECTIVES:** We aimed to investigate for the first time the expression pattern of AMPs in lesions of LS as compared with healthy skin. **METHODS:** Twenty-four women with LS as well as 10 healthy women were included in the study. In order to assess the expression of human beta-defensin (hBD)-1, hBD-2, hBD-3, psoriasin (S100A7), the cathelicidin LL-37 and RNase 7, real-time reverse transcriptase-polymerase chain reaction and immunohistochemistry were performed on skin specimens obtained from lesional and healthy skin of the genital region, respectively. **RESULTS:** Median hBD-2 mRNA levels observed in LS were significantly higher than in controls (0.15 vs. 0.008; $P = 0.0037$). Moreover, psoriasin (98.2 vs. 28.1; $P = 0.0052$) mRNA expression was significantly higher in LS lesions as compared with controls. Significant differences in mRNA expression of hBD-2 and psoriasin were also confirmed by immunohistochemistry. For hBD-1, hBD-3, LL-37 and RNase 7, levels did not differ significantly or were significant only at the gene level but not protein level. **CONCLUSIONS:** We have demonstrated that hBD-2 and psoriasin expression levels in lesional skin of patients with LS are significantly increased when compared with healthy controls. Whether this observation simply reflects an innate defence response caused by an increased risk of local infection, or whether our data indicate a pathogenetic role of AMPs in LS, will be addressed in future studies.

Anatomy / Basic Science

Plasma membrane estrogen receptors.

Levin ER.
Trends Endocrinol Metab. 2009 Sep 23. [Epub ahead of print]

It is now firmly established that estrogen and all sex steroid receptors exist in discrete cellular pools outside the nucleus. Estrogen receptors (ER) have been localized to the plasma membrane where both ERalpha and ERbeta function in a wide variety of cells and organs. ERs have also been found in discrete cytoplasmic organelles including mitochondria and the endoplasmic reticulum. In ligand-dependent fashion, each ER pool contributes to the overall, integrated effects of estrogens producing biological outcomes. This review highlights the recent work establishing new roles and targets of membrane ER signaling. Such actions include prevention of vascular injury or cardiac hypertrophy, sexual behavior and

pain perception mediated through the central nervous system, osteoblast survival, and fluid resorption in the colon.

Estradiol ameliorates diabetes-induced changes in vaginal structure of db/db mouse model.

Cushman TT, Kim N, Hoyt R, Traish AM.

J Sex Med. 2009 Sep;6(9):2467-79.

INTRODUCTION: Women with diabetes experience diminished genital arousal, reduced vaginal lubrication, vaginal atrophy, dyspareunia, and increased infections. Limited studies are available investigating the effects of diabetic complications on the vagina. **AIMS:** The goals of this study were to investigate type 2 diabetes-induced changes in vaginal structure, and to determine if estradiol treatment ameliorates these changes. **METHODS:** Eight-week-old female diabetic (db/db) mice (strain BKS**Cg-m*+/*+*Lepr(db)/J) and age-matched control normoglycemic female littermates were used to investigate the effects of type 2 diabetes on vaginal tissue structural integrity. Diabetic animals were divided into two subgroups: diabetic treated with vehicle only and diabetic treated with pellets containing estradiol. At 16 weeks, the animals were sacrificed, and the vaginal tissues were excised and analyzed by histological and immunohistochemical methods to assess diabetes-induced changes in vaginal tissue and the extent by which these parameters are restored by estradiol treatment. **MAIN OUTCOME MEASURES:** The effects of type 2 diabetes and estradiol supplementation were investigated on vaginal histoarchitecture. **RESULTS:** Diabetic animals exhibited high blood glucose levels (>600 mg/dL), increased body weight (43.0 +/- 6.0 g vs. 24.4 +/- 2.0 g), and reduced plasma estradiol levels (65.5 +/- 6.6 pg/mL vs. 80.77 +/- 13.2 pg/mL) when compared to control animals. Diabetes resulted in significant thinning of the epithelium ($P \leq 0.05$), marked decrease in the muscularis area ($P \leq 0.05$), distinct truncation of elastic fibers, and significant reduction of the nitrergic immunoreactive nerve fibers ($P \leq 0.05$). Treatment of diabetic animals with estradiol restored epithelial thickness ($P \leq 0.05$), muscularis area ($P \leq 0.05$), and elastic fiber distribution, and partially restored the density of nitrergic nerve fibers. **CONCLUSIONS:** The data in this study demonstrate that type 2 diabetes disrupts vaginal structural integrity and that estradiol supplementation ameliorates the diabetes-induced vaginal pathology.