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This newsletter is quarterly and contains abstracts from medical journals published between September and December 2002 (abstracts presented at scientific meetings may also be included). Please direct any comments regarding this newsletter to [chris@nva.org](mailto:chris@nva.org).

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Differential characterization of women with vulvar vestibulitis syndrome.

Witkin SS, Gerber S, Ledger WJ

Am J Obstet Gynecol 2002 Sep;187(3 Pt 1):589-94

OBJECTIVE: We differentiated women with vulvar vestibulitis syndrome into subgroups on the basis of the time of symptom onset, a history of recurrent vulvovaginal candidiasis, and the interleukin-1 receptor antagonist gene polymorphism. Study Design: One hundred sixty-two consecutive patients with strictly defined vulvar vestibulitis syndrome were asked to fill out a questionnaire with the assistance of their gynecologist. A buccal sample was collected from each subject for the analysis of interleukin-1 receptor antagonist gene polymorphism; vaginal and vestibular microbial investigations were performed. RESULTS: Symptoms began with the first act of coitus in 20.4% of patients. A history of a recurrent Candida vulvovaginal infection was reported in 42.6% of patients; 25.9% of the patients were positive for the homozygous interleukin-1 receptor antagonist 2,2 genotype. Women with primary vulvar vestibulitis syndrome differed from women with secondary vulvar vestibulitis syndrome; women with primary vulvar vestibulitis syndrome were younger at the time of the onset of the symptoms (23.8 vs 31.2 years,  $P < .0001$ ) and had never been pregnant (84.8% vs 61.2%,  $P < .0001$ ). Women with a history of recurrent Candida vulvovaginitis differed from the other subjects by having a higher frequency of constant vestibular pain (40.6% vs 20.4%,  $P = .005$ ), a vaginal discharge (79.7% vs 45.2%,  $P < .0001$ ), and dysuria (62.3% vs 29.0%,  $P = .0001$ ). Women who were homozygous for interleukin-1 receptor antagonist 2,2 genotype had an earlier onset of symptoms (26 years) than did women who were allele 1 homozygotes (31.3 years,  $P < .05$ ). They also had a shorter duration of symptoms (4.1 vs 5.9 years,  $P < .05$ ) and a higher frequency of allergy (47.6% vs 23.4%,  $P = .002$ ). Human

papillomavirus in the vaginal vestibule occurred at a greater frequency in women who were homozygous for interleukin-1 receptor antagonist 2,2 genotype. CONCLUSION: Subgroups of women with vulvar vestibulitis syndrome may be differentiated by symptomatic and genetic variables.

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Characteristics and initial diagnoses in women presenting to a referral center for vulvovaginal disorders in 1996-2000.

Hansen A, Carr K, Jensen JT

J Reprod Med 2002 Oct;47(10):854-60

OBJECTIVE: To describe the demographics, presenting symptoms, physical examination and laboratory findings, and initial diagnoses in a cohort of women referred for evaluation of vulvovaginal problems. STUDY DESIGN: Descriptive review of medical records of new patients referred for evaluation of vulvar problems between January 1, 1996, and December 31, 1999. Electronic medical records and other documents were manually abstracted. RESULTS: Three hundred twenty-two women met the study criteria. The majority were Caucasian (93.8%) and married (63.9%). The mean age was 41 years, with a range of 13-88. The majority reported at least one vaginal delivery (72.9%) or cesarean section (10.6%). The most common symptoms were vulvar pain (86.3%), dyspareunia (70.8%), itching (36.0%) and skin changes (18.0%). Most patients received a diagnosis in more than one evaluation category. Prevalent diagnoses included Bartholin fossa pain (12.1%), vulvar vestibulitis (19.9%), restriction and fissuring of the posterior labial commissure (20.1%), dysesthetic vulvodinia (32.3%), pelvic floor dysfunction (39.8%) and dermatologic conditions (47.5%). CONCLUSION: Women presenting for evaluation of vulvar disorders represent a heterogeneous population. Among women with vulvar pain, abnormalities of the skin and pelvic floor are common and should be ruled out prior to making a diagnosis of vulvar vestibulitis or dysesthetic vulvodinia.

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Victimization in patients with vulvar dysesthesia/vestibulodynia. Is there an increased prevalence?

Dalton VK, Haefner HK, Reed BD, Senapati S, Cook A

J Reprod Med 2002 Oct;47(10):829-34

OBJECTIVE: To examine the prevalence of physical or sexual violence victimization among women referred to a specialty clinic for management of vulvar dysesthesia/vestibulodynia as compared to a healthy gynecology clinic population. STUDY DESIGN: The subjects in this case-control study were women who had completed routine questionnaires prior to presentation to the University of Michigan Center for Vulvar Diseases. Study subjects were all given a diagnosis of vulvar dysesthesia/vestibulodynia. Women without complaints of vulvar pain presenting to a gynecology clinic were enrolled as controls. Information was obtained from the control subjects using a questionnaire similar to the history forms completed by the study group. RESULTS: Comparisons were made between 242 patients with vulvar dysesthesia/vestibulodynia

presenting to a specialty clinic and 113 controls. Cases were more likely to be Caucasian, to be married and to have a higher household income than controls but reported less drug or alcohol abuse and a lower frequency of sexual intercourse. After controlling for possible confounders, no relationship between sexual assault and the presence of vulvar dysesthesia/ vestibulitis was found. CONCLUSION: The prevalence of victimization was not higher in patients with vulvar dysesthesia/ vestibulodynia as compared to the control population after controlling for potential confounding variables.

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Clinical management of vulvodynia.

Glazer HI, Ledger WJ

Reviews in Gynaecological Practice, Volume 2, Issues 1-2, pgs 83-90

Vulvodynia, also known as burning vulva syndrome, is characterised by sensory abnormalities of the vulva and the surrounding tissue, such as an unpleasant burning and itching sensation, or a painful response to a stimulus that is not usually painful such as sexual intercourse or the touch of a cotton swab. Organic vulvodynia is often treatable once a cause has been established. Idiopathic vulvodynia, which consists of vulvar dysesthesia or vulvar vestibulitis syndrome, often exists in conjunction with organic vulvodynia. Both entities should be treated concurrently, if possible. Several treatment methods exist for idiopathic vulvodynia and most may be used in conjunction with each other. Treatment options that are less invasive are often tried first, including hygienic and dietary changes, surface electromyographic biofeedback, and medications. Surgery, effective only for vulvar vestibulitis syndrome and usually considered only for women refractory to other treatments, can be combined with other treatments (interferon, and sEMG biofeedback for example) to increase effectiveness. A pathway of treatment options is presented.

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Vulvar vestibulitis: a reappraisal.

Rosenman SD

Conn Med 2002 Oct;66(10):589-93

Vulvar vestibulitis is still an enigma. There is much confusion concerning the terminology, symptoms, etiology, and treatment of the syndrome. A medline search on Vulvar Vestibulitis was completed from 1989 to 2001. Twenty-six different treatment modalities are listed. Some studies have shown a significant increase in intraepithelial nerve endings in vulvar vestibulitis. The most successful curative treatment seems to be surgery, which would postulate that removal of the nerve fibers eradicates the discomfort and symptoms of the disease. Randomized control trials need to be undertaken to ascertain the efficacy of treatments of this debilitating disease.

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Web-enabled Glazer surface electromyographic protocol for the remote, real-time assessment and rehabilitation of pelvic floor dysfunction in vulvar vestibulitis syndrome. A case report.

Glazer HI, Marinoff SC, Sleight IJ

J Reprod Med 2002 Sep;47(9):728-30

**BACKGROUND:** The browser-based software for the Glazer pelvic floor muscle surface electromyography (sEMG) protocol can be used for remote, real-time assessment and treatment over the Internet. **CASE:** The initial application of this system is reported for a patient meeting clinical diagnostic criteria for vulvar vestibulitis syndrome. The patient underwent pelvic floor muscle sEMG evaluation in the Washington, D.C., office of the second author, remotely controlled by the first author from his office in New York City. Pelvic muscle sEMG findings were consistent with previous reports on vestibulitis patients, and rehabilitative exercises were prescribed. Follow-up evaluations and home training normalized the sEMG and resulted in elimination of pain. **CONCLUSION:** Remote, real-time pelvic floor muscle sEMG in the diagnosis and treatment of vulvar vestibulitis is a novel application of telemedicine with demonstrated efficacy, permitting this technology to be available to all practitioners.

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The female sexual pain disorders: genital pain or sexual dysfunction?

Binik YM, Reissing E, Pukall C, Flory N, Payne KA, Khalife S

Arch Sex Behav 2002 Oct;31(5):425-9

Vaginismus and dyspareunia have been typically classified as sexual dysfunctions. In practice and research, this conceptualization has led to a focus on sexual and interpersonal issues after biological causes were excluded. Although this approach has been very useful, it has not led to significant theoretical or therapeutic progress in the last 20 years. We propose a reconceptualization of vaginismus and dyspareunia as pain disorders that interfere with sexuality rather than as sexual disorders characterized by pain. This reconceptualization focuses the clinician and researcher on the central phenomenon-pain. It also suggests new approaches to research and treatment. Data from diagnostic, etiologic, and therapeutic studies will be presented to illustrate these points.

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Clitoral priapism: a rare condition presenting as a cause of vulvar pain.

Medina CA

Obstet Gynecol 2002 Nov;100(5 Pt 2):1089-91

**BACKGROUND:** Priapism of the clitoris is a rare condition associated with prolonged erection of the clitoris causing engorgement, swelling,

and pain to the clitoris and immediate adjacent area. CASE: A 47-year-old woman presented complaining of vulvar and clitoral pain. Self-reported findings of a swollen and tender clitoris had been confirmed by physical examination during an episode of priapism, otherwise there were no abnormal findings on routine evaluation. The history and findings of prolonged clitoral swelling, tenderness, and pain of the clitoris and adjacent area were considered consistent with clitoral priapism, and discovered to be attributed to the use of trazodone hydrochloride, a heterocyclic antidepressant. The patient was initially treated with imipramine hydrochloride; however, it was the withdrawal of the medication instigating the condition that was the focal point in its management. CONCLUSION: Priapism of the clitoris is a condition that may develop during therapy with certain medications, specifically those possessing a strong alpha-adrenergic blockade. Conditions altering blood flow to the clitoris may also predispose to developing this condition. Familiarity with this condition and a high index of suspicion are paramount in establishing a diagnosis.

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The prevalence of interstitial cystitis in gynecologic patients with pelvic pain, as detected by intravesical potassium sensitivity.

Parsons CL, Dell J, Stanford J, Bullen M

Am J Obstet Gynecol 2002 Nov;187(5):1395-1400

OBJECTIVE: The purpose of this study was to determine the prevalence of interstitial cystitis in a large number of gynecologic patients with pelvic pain versus control subjects, as indicated by a positive result on a potassium sensitivity test. Study Design: Gynecologists at four US medical centers administered the potassium sensitivity test to consecutive unselected patients with pelvic pain and control subjects. Before testing, each patient with pelvic pain was given an initial clinical diagnosis on the basis of the chief symptomatic complaint(s) and was surveyed for urologic symptoms. RESULTS: Of 244 patients with pelvic pain, 197 patients (81 %) had a positive result from a potassium sensitivity test. Positive potassium sensitivity test rates were comparable across all four sites and all clinical diagnoses that included endometriosis, vulvodynia (vulvar vestibulitis), and pelvic pain. Urologic symptoms were reported by 84% of patients, but only 1.6% of the patients had received an initial diagnosis of interstitial cystitis. None of the 47 control subjects were tested positive with the potassium sensitivity test. CONCLUSION: Interstitial cystitis may be a common unrecognized cause of pelvic pain in gynecologic patients and deserves greater, if not primary, consideration in the differential diagnosis of pelvic pain.

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Essential vulvodynia (vulval pain).

Murphy D, Redman C, Thomas E

Clin Evid 2002 Jun;(7):1663-5

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Vulvar vestibulitis: a real syndrome?

Marin G, Dennerstein G

J Reprod Med 2002 Sep;47(9):775; discussion 775-6

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Pudendal nerve terminal motor latency measurements: what they do and do not tell us.

Hill J, Hosker G, Kiff ES

Br J Surg 2002 Oct;89(10):1268-9

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#### VULVOVAGINAL INFECTION AND DERMATOSES

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Developments in vulvovaginal care.

Stewart EG

Curr Opin Obstet Gynecol 2002 Oct;14(5):483-8

Clinical studies on the myriad benign diseases of the vulva and vagina have long been outnumbered by emphasis on other areas of obstetrics and gynecology. The complexity of vulvovaginal diseases emerges in the recent literature. As clinicians embrace available knowledge, women's health will improve. This review encompasses current developments in candida, bacterial vaginosis, lichen sclerosus and vulvodynia.

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Lichen sclerosus and other conditions mimicking vulvovaginal candidiasis.

Nyirjesy P

Curr Infect Dis Rep 2002 Dec;4(6):520-524

For many women with chronic vulvovaginal symptoms, overdiagnosis of vulvovaginal candidiasis (VVC) is an unfortunate tendency. In women with chronic vulvar itching or burning, a vulvar non-neoplastic epithelial disorder is a relatively frequent diagnosis. Although controversy persists about the nomenclature for these disorders, there seems to be a relatively clear consensus with lichen sclerosus. This chronic inflammatory skin disease affects primarily the female vulvar and perianal areas. Left untreated, it may lead to chronic scarring of the vulva with an associated loss of architecture. The etiology remains unknown, although infectious, genetic, and autoimmune causes have been suggested. Most patients will respond to potent topical corticosteroids. Treatment of associated conditions such as atrophic vaginitis or complicated VVC is sometimes necessary. Surgery should be considered in patients with severe scarring.

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Pathogenesis of recurrent vulvovaginal candidiasis.

Sobel JD

Curr Infect Dis Rep 2002 Dec;4(6):514-519

Recurrent vulvovaginal candidiasis (RVVC) is by no means uncommon and is a source of considerable physical suffering, in addition to serving as a major therapeutic challenge. The syndrome is multifactorial in etiology, hence management strategies must recognize the complex etiologic pathways. Considerable progress has been made in identifying secondary causes, including biologic and host factors. Specifically, Candida microbiologic studies have revealed that azole resistance in Candida albicans is rare and infection by less sensitive non-albicans Candida species is uncommon. At least half the women with RVVC have no identifiable host or microbial predisposing factors, and an immune-based hypothesis has been generated.

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#### BASIC SCIENCE

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c-Fos expression in the spinal cord after acute sacral segmental nerve stimulation.

Ishigooka M, Nakada T, Hashimoto T, Zermann DH, Schmidt RA

Neurourol Urodyn 2002;21(5):495-501

AIMS: Sacral nerve stimulation (SNS) can provide subjective and objective relief of pelvic pain and chronic voiding symptoms, but its mechanism is poorly understood. It is well known that a noxious stimulus applied to one part of the body can reduce the response to a subsequent stimulus elsewhere in the body. This phenomenon, known as diffuse noxious inhibitory controls (DNIC), seems to be the mechanism by which pain can be reduced by concurrent noxious stimulation. METHODS: On the basis of the DNIC concept, we investigated the expression of a protein product of proto-oncogene c-Fos (c-Fos) in the rat spinal cord after acute electrical stimulation of the sacral segmental nerve with or without lower urinary tract irritation. Adult male Sprague-Dawley rats were treated either by sacral nerve stimulation (SNS) from the S1 sacral foramen or chemical irritation of the lower urinary tract (LUT) or both. Rats were perfused transcardially, and spinal cords were removed and processed for c-Fos immunohistochemistry. c-Fos expression in the central nervous system was detected by immunohistochemistry by using the avidin-biotin technique. The number of c-Fos-positive cells and their locations in the spinal cord were evaluated. RESULTS: SNS and LUT irritation resulted in significant increases in c-Fos-positive cells in L6 and S1 spinal segments. In the animals treated by SNS and LUT irritation, counts of c-Fos-positive cells in L6 and S1 segments were significantly smaller than expected. Distribution and number of c-Fos-positive cells

in rats that received SNS and LUT irritation were almost the same as those induced by SNS alone in the S1 segment. CONCLUSIONS: SNS alone caused a near maximal response in c-Fos expression such that adding LUT irritation did not cause a linear increase in c-Fos. Subsequent LUT irritation could not induce additional expression of c-Fos within the spinal cord.