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This newsletter is quarterly and contains abstracts from medical journals published between September and December 2004 (abstracts presented at scientific meetings may also be included). Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia / Pain

Altered distribution of mannose-binding lectin alleles at exon I codon 54 in women with vulvar vestibulitis syndrome.
Babula C, Danielsson I, Sjoberg I, Ledger WJ, Witkin SS
American Journal of Obstetrics and Gynecology, Vol 191, Issue 3, Sept 2004, Pages 762-6

Objective: Mannose-binding lectin (MBL) is active in the innate immune defense against microorganisms. In this study, we determined whether vulvar vestibulitis syndrome, a disorder of unknown etiology, was associated with an altered distribution of MBL alleles. Study Design: Buccal swabs were obtained from women with vulvar vestibulitis syndrome in New York (62) and from 2 cities in Sweden (60), as well as control women in New York (48) and Sweden (51). DNA was tested for a single nucleotide polymorphism at codon 54 in exon I by polymerase chain reaction, endonuclease digestion, and gel electrophoresis. Blood samples were also obtained from the New York women and tested by ELISA for plasma MBL concentrations. The relationships between genotype, allele frequencies, blood MBL levels, and diagnosis were analyzed by Fisher exact test and one-way analysis of variance. Results: The variant MBL allele, MBL*B, was detected in 35.5% and 26.7% of vulvar vestibulitis patients from New York and Sweden, respectively. Only 12.5% of New York controls (P = .007) and 9.8% of Swedish controls (P=.01) were MBL*2-positive. All women, with one exception, who were positive for MBL*B were MBL*A/MBL*B heterozygotes. Women who carried MBL*B had almost a 10-fold reduction in median plasma MBL concentrations (278 ng/mL), as opposed to women who were MBL*A homozygotes (1980 ng/mL) (P < .0001). Conclusion: MBL*B carriage and reduced plasma MBL levels are more common in women with vulvar vestibulitis syndrome than in control patients, and may contribute to symptomatology in a subset of patients.

The major histopathologic characteristics in the vulvar vestibulitis syndrome.
Halperin R, Zehavi S, Vaknin Z, Ben-Ami I, Pansky M, Schneider D
Gynecol Obstet Invest. 2004 Nov 11;59(2):75-79

Objective: In order to better understand the etiology of the vulvar vestibulitis syndrome, we examined the histopathologic parameters in vestibular mucosa, and compared the findings in specimens obtained from women with vulvar vestibulitis with those obtained from the control group. Study Design: Specimens of vestibulitis were obtained from 24 patients, undergoing circumferential vestibulectomy under general anesthesia due to the symptoms and signs consistent with vulvar vestibulitis. Control specimens were obtained from 16 women, without symptoms or signs of vulvar vestibulitis, undergoing reconstructive introital surgery due to roomy vagina, rectocele or painful episiotomy. All vestibular tissue specimens

were examined for intensity of inflammation, extension of inflammatory cells into the epithelium, vascular proliferation, the presence of mast cells and proliferation of peripheral nerve bundles. Results: No significant difference was found regarding the degree of inflammation, the extension of inflammatory cells into the epithelium, the vascular proliferation and the presence of mast cells while comparing the study and the control groups. The only histopathologic feature, differentiating the patients with vulvar vestibulitis from the control group, was the proliferation of peripheral nerve bundles found in 19 out of 24 (79.1%) specimens expressing vestibulitis and in none of 16 control specimens ($p < 0.0001$). Conclusion: Our results, therefore, support the existence of peripheral nerve hyperplasia in vestibular tissue obtained from patients with vulvar vestibulitis, and exclude the role of active inflammation or mast cells as probable etiologies for the vulvar vestibulitis syndrome.

Pudendal neuropathy is best determined by full neurophysiologic assessment.
O'Brien C, O'Herlihy C, O'Connell PR
Am J Obstet Gynecol. 2004 Nov;191(5):1836

Pudendal nerve decompression in perineology: a case series.
Beco J, Climov D, Bex M
BMC Surg. 2004 Oct 30;4(1):15

BACKGROUND: Perineodynia (vulvodynia, perineal pain, proctalgia), anal and urinary incontinence are the main symptoms of the pudendal canal syndrome (PCS) or entrapment of the pudendal nerve. The first aim of this study was to evaluate the effect of bilateral pudendal nerve decompression (PND) on the symptoms of the PCS, on three clinical signs (abnormal sensibility, painful Alcock's canal, painful "skin rolling test") and on two neurophysiological tests: electromyography (EMG) and pudendal nerve terminal motor latencies (PNTML). The second aim was to study the clinical value of the aforementioned clinical signs in the diagnosis of PCS. METHODS: In this retrospective analysis, the studied sample comprised 74 female patients who underwent a bilateral PND between 1995 and 2002. To accomplish the first aim, the patients sample was compared before and at least one year after surgery by means of descriptive statistics and hypothesis testing. The second aim was achieved by means of a statistical comparison between the patient's group before the operation and a control group of 82 women without any of the following signs: prolapse, anal incontinence, perineodynia, dyschesia and history of pelvi-perineal surgery. RESULTS: When bilateral PND was the only procedure done to treat the symptoms, the cure rates of perineodynia, anal incontinence and urinary incontinence were 8/14, 4/5 and 3/5, respectively. The frequency of the three clinical signs was significantly reduced. There was a significant reduction of anal and perineal PNTML and a significant increase of anal richness on EMG. The Odd Ratio of the three clinical signs in the diagnosis of PCS was 16,97 (95% CI = 4,68 - 61,51). CONCLUSION: This study suggests that bilateral PND can treat perineodynia, anal and urinary incontinence. The three clinical signs of PCS seem to be efficient to suspect this diagnosis. There is a need for further studies to confirm these preliminary results.

Incidence, severity, and determinants of perineal pain after vaginal delivery: A prospective cohort study.
Macarthur AJ, Macarthur C
American Journal of Obstetrics and Gynecology, Vol 191, Issue 4, Oct 2004, Pages 1199-1204

Objectives: The purpose of this study was to determine the frequency of perineal pain in the 6 weeks after vaginal delivery and to assess the association between perineal trauma and perineal pain.
Study design: This was a prospective cohort study of parturients at 1 day, 7 days,' and 6 weeks' post partum in an academic tertiary obstetric unit in Toronto, Canada. Four hundred forty-four women were followed up, including women with an intact perineum (n = 84), first-/second-degree tears (n = 220), episiotomies (n = 97), or third-/fourth-degree tears (n = 46). Primary outcome was the incidence of perineal pain on day of interview; secondary outcomes were pain score measurements and interference with daily activities. Results: Perineal trauma was more common among primiparous women, those with

operative vaginal deliveries, and those with epidural analgesia during the second stage of labor. The incidence of perineal pain among the groups during the first week was intact perineum 75% (day 1) and 38% (day 7); first-/second-degree tears 95% and 60%; episiotomies 97% and 71%; and third-/fourth-degree tears 100% and 91%. By 6 weeks, the frequency of perineal pain was not statistically different between trauma groups. Conclusion: Acute postpartum perineal pain is common among all women. However, perineal pain was more frequent and severe for women with increased perineal trauma.

Vaginal dilator therapy-an outpatient gynaecological option in the management of dyspareunia.
O Idama D W Pring T
J Obstet Gynaecol. 2000;20(3):303-5

The management of 18 women complaining of superficial dyspareunia is reviewed. Primary treatment consisted of self-vaginal dilatation using graduated glass dilators on an outpatient basis. All patients were given verbal explanation and written instructions. Treatment was considered successful with dilator therapy in 14 (77.8%) women. Three (16.7%) women required additional therapy in the form of surgery or psychotherapy. We conclude that in selected cases, self-vaginal dilator usage on an outpatient basis is effective primary therapy for superficial dyspareunia.

EAU guidelines on chronic pelvic pain.
Fall M, Baranowski AP, Fowler CJ, Lepinard V, Malone-Lee JG, Messelink EJ, Oberpenning F, Osborne JL, Schumacher S
Eur Urol. 2004 Dec;46(6):681-689

OBJECTIVES:: On behalf of the European Association of Urology (EAU) guidelines for diagnosis, therapy and follow-up of chronic pelvic pain patients were established. METHOD:: Guidelines were compiled by a working group and based on current literature following a systematic review using MEDLINE. References were weighted by the panel of experts. RESULTS:: The full text of the guidelines is available through the EAU Central Office and the EAU website (). This article is a short version of this text and summarises the main conclusions from the guidelines on management of chronic pelvic pain. CONCLUSION:: A guidelines text is presented including chapters on prostate pain and bladder pain syndromes, urethral pain, scrotal pain, pelvic pain in gynaecological practice, role of the pelvic floor and pudendal nerve, general treatment of chronic pelvic pain and neuromodulation. These guidelines have been drawn up to provide support in the management of the large and difficult group of patients suffering from chronic pelvic pain.

Vulvar Dermatoses

Focused ultrasound therapy of vulvar dystrophies: A feasibility study.
Li C, Bian D, Chen W, Zhao C, Yin N, Wang Z
Obstet Gynecol. 2004 Nov;104(5):915-921

OBJECTIVE: To explore the feasibility and efficacy of focused ultrasound treatment of squamous hyperplasia and lichen sclerosus. METHODS: A simple randomized phase 2 study was conducted in which a total of 76 patients (45 with squamous hyperplasia and 31 with lichen sclerosus) were treated with focused ultrasound therapy from 1999 to 2002. Before and after the treatment, the therapeutic responses were evaluated based on changes in clinical symptoms and signs. Pre- and posttreatment biopsy specimens were also assessed through the light and electron microscopic examinations. The positive expressions of CD34 and myelin basic protein (MBP) tests with the strepavidin-peroxidase immunohistochemistry method were used to evaluate the therapeutic response. Statistical analysis was performed using chi(2) (McNemar chi(2)) test and t test. RESULTS: After the ultrasound treatment,

clinical symptoms were dramatically improved with a total response rate of 94.74%. Three to 6 months later the skin of treated areas returned to normal appearance. In the 2-year follow-up, 49 of 76 cases (32 squamous hyperplasia and 17 lichen sclerosus) were cured, 23 (11 squamous hyperplasia and 12 lichen sclerosus) improved and 4 (2 squamous hyperplasia and 2 lichen sclerosus) persisted. The positive expressions of CD34 and MBP after treatment increased significantly at the treated region ($P < .05$). No major complications occurred. CONCLUSION: Vulvar dystrophy could be effectively treated with focused ultrasound therapy. This approach appears to be a new promising treatment method, although further studies are still needed.

Macrolactam immunomodulators (tacrolimus and pimecrolimus): new horizons in the topical treatment of inflammatory skin diseases.
Grunwald MH, Ben Amitai D, Amichai B
J Dermatol. 2004 Aug;31(8):592-602

Tacrolimus and pimecrolimus are new macrolactam immunomodulators which were developed for the treatment of inflammatory skin diseases, mainly atopic dermatitis. In this article, we review the pharmacologic properties of the drugs, their side effects, and their clinical uses.

Infectious Disease

Trends in prescribing for vulvovaginal candidiasis in the United States.
McCaig LF, McNeil MM
Pharmacoepidemiol Drug Saf. 2004 Mar 19

PURPOSE: To describe trends in visits to office-based physicians in the United States by females 15-64 years of age for vulvovaginal candidiasis and related antifungal prescribing. Since January 1991, intravaginal antifungal medications have been available over-the-counter in the United States to treat vulvovaginal candidiasis. METHODS: Data from the 1985 through 2001 National Ambulatory Medical Care Surveys (NAMCS) were examined. NAMCS is an annual national probability sample survey that collects data on the utilization of services provided by office-based physicians. RESULTS: The average annual visit rates for symptoms of vaginitis and a diagnosis of vulvovaginal candidiasis decreased by 55 and 72%, respectively. The intravaginal antifungal prescribing rate for vulvovaginal candidiasis declined by 41%. No trend was found for total antifungal prescribing; however, during the late 1990s, fluconazole was prescribed at approximately one-third of visits with a diagnosis of vulvovaginal candidiasis. CONCLUSION: These data suggest an increased trend in self-diagnosis and use of over-the-counter intravaginal antifungal medications. The shift from prescribing intravaginal antifungal preparations to fluconazole raises concern about the possible development of azole drug resistance. Educational efforts are needed to counter potential misuse of these medications that may contribute to increased infection with innately azole resistant non-albicans Candida species and chronic infection.

Basic Science

Pattern of sensory innervation of the perineal skin in the female rat.
Cruz Y, Zempoalteca R, Angelica Lucio R, Pacheco P, Hudson R, Martinez-Gomez M
Brain Res. 2004 Oct 22;1024(1-2):97-103

Here we describe the nerves innervating the perineal skin together with their sensory fields in the adult female rat. Electrophysiological recording showed that the lumbosacral and L6-S1 trunks, in part by way of the sacral plexus, transmit sensory information from the perineal skin via four nerves: the

viscerocutaneous branch of the pelvic nerve innervating the skin at the midline between the vaginal opening and anus, the sensory branch of the pudendal nerve innervating the clitoral sheath, the distal perineal branch of the pudendal nerve innervating a broad area of skin adjacent to the vaginal opening and anus, and the proximal perineal branch of the sacral plexus innervating a broad area of skin adjacent to the clitoris and vaginal opening. The sensory fields of three of these nerves overlapped to some degree: the viscerocutaneous branch of the pelvic and the distal perineal branch of the pudendal nerves at the midline skin between the vaginal opening and the anus, and the distal perineal branch of the pudendal nerve and the proximal perineal branch of the sacral plexus at the skin lateral to the vaginal opening. Such overlap might provide a safeguard helping to ensure that somatosensory input from the perineal region important for triggering reproductive and nonreproductive reflexes reaches the CNS.