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This newsletter is quarterly and contains abstracts from medical journals published between December 2005 and March 2006 (abstracts presented at scientific meetings may also be included). Please direct any comments regarding this newsletter to chris@nva.org.

Vulvodynia / Pain

Satyriasis: the antiquity term for vulvodynia?

McElhiney J, Kelly S, Rosen R, Bachmann G
J Sex Med 2006 Jan;3(1): 161-3

From ancient times, through the Middle Ages, and well into the 19th century, physicians concentrated on catastrophic medical conditions and illnesses rather than on quality of life issues. Wars, plagues, and pestilence left little time, energy, or concern for "discomfort" problems. Therefore, it is not surprising that women's conditions that caused distressing symptoms but fell short of major morbidity and mortality were not given a prominent position in medicine until relatively recently. This is especially the case with vulvodynia, a condition that has been reported to affect approximately 15% (and in some studies up to 27%) of the female population at some point in their lives. Despite its high prevalence, this condition was not discussed or reported in traditional medical textbooks until the end of the 1800s. Now, we propose another viewpoint on when the first description of vulvodynia appeared; that is, that vulvodynia was described as far back as the 1st century CE. From our review of the ancient medical literature, we believe that the condition described by Soranus as "satyriasis in females" was actually vulvodynia.

Chronic vulvar and other gynecologic pain: prevalence and characteristics in a self-reported survey.

Bachmann GA, Rosen R, Arnold LD, Burd I, Rhoads GG, Leiblum SR, Avis N
J Reprod Med 2006 Jan;51(1):3-9

OBJECTIVE: To characterize and assess the prevalence of chronic gynecologic pain and, more specifically, chronic vulvar pain. **STUDY DESIGN:** A questionnaire was mailed to women aged 18-80 years who were ambulatory patients at an academic multidisciplinary practice. Quality of life, health history, obstetric and gynecologic history, and pain symptoms were assessed. **RESULTS:** Of the 4,872 surveys mailed to deliverable addresses, 36.8% were returned. The population was primarily Caucasian (83%), with an average age of 50.2 years. Approximately 4% of respondents reported a history of vulvar pain in the 6 months preceding the survey, and 17% reported other types of chronic gynecologic pain. Women reporting vulvar and nonvulvar pain were 2 times as likely as asymptomatic women to report a history of depression and vaginal infections, a poorer quality of life ($p < 0.001$) and greater stress. Dyspareunia and pain with daily activities were reported more frequently by women with vulvar pain than by women with non-vulvar gynecologic pain. **CONCLUSION:** The prevalence of vulvar pain in this study was lower than previously reported. Chronic gynecologic pain, and vulvar pain in particular, affects quality of life on both intimate and social levels. Self-reported stress and vaginal infections were the strongest correlates of chronic vulvar pain.

Vulvodynia: characteristics and associations with co-morbidities and quality of life.

Arnold LD, Bachmann GA, Rosen R, Kelly S, Rhoads GG
Obstet Gynecol 2006 Mar;107(3):617-624

OBJECTIVE: This case-control survey compared health history and health care use of women with vulvodynia with a control group reporting absence of gynecologic pain. **METHODS:** Women with a clinically assessed diagnosis of vulvodynia and asymptomatic controls were matched for age and mailed a confidential survey that evaluated demographics, health history, use of the health care system, and history of vulvodynia. Participants were all current or former ambulatory patients within a university health care system. **RESULTS:** Of the 512 questionnaires mailed to valid addresses, 70% (n = 91) of cases and 72% (n = 275) of controls responded, with 77 cases and 208 controls meeting eligibility criteria. Women with vulvodynia reported a substantial negative impact on quality of life, with 42% feeling out of control of their lives and 60% feeling out of control of their bodies. Forty-one percent indicated a severe impact on their sexual lives. When co-morbidities were evaluated individually and adjusted for age, fibromyalgia (odds ratio 3.84, 95% confidence interval 1.54-9.55) and irritable bowel syndrome (odds ratio 3.11, 95% confidence interval 1.60-6.05) were significantly associated with vulvodynia. On a multivariate level, vulvodynia was correlated with a history of chronic yeast vaginitis and urinary tract infections. **CONCLUSION:** This survey highlights the psychological distress associated with vulvodynia and underscores the need for prospective studies to investigate the relationship between chronic bladder and vaginal infections as etiologies for this condition. As well, the association of vulvodynia with other comorbid conditions, such as fibromyalgia and irritable bowel syndrome, needs to be further evaluated. **LEVEL OF EVIDENCE:** II-2.

Dyspareunia and urinary sensory symptoms in India: population-based study.

Padmadas SS, Stones RW, Matthews Z
J Sex Med 2006 Jan;3(1):114-20

INTRODUCTION: Population level estimates of sexual dysfunction in less developed settings where sexuality is not openly discussed or is culturally constrained are lacking. **AIM:** To determine the prevalence of dyspareunia and identify associated symptoms and sociocultural factors. **METHODS:** Data from a population-based national level family health sample survey conducted in Indian states from 1998 to 1999 which collected sexual and reproductive health information from 84,644 currently married women. The main outcome measure was dyspareunia. **RESULTS:** The overall prevalence of dyspareunia was 12.6%, with a higher prevalence in the central region, among newly married and younger women, among Muslims, rural residents, and among nonusers or traditional contraceptive method users. Dyspareunia was significantly more common among respondents who had urinary sensory symptoms when compared with their counterparts (adjusted odds ratio: 6.57, 95% confidence interval: 6.28, 6.87). **CONCLUSION:** Dyspareunia prevalence and the associated symptoms reported in this analysis could be underestimated because of possible underreporting. There is a substantial hidden burden of sexual health problems especially affecting younger women.

Interstitial cystitis: cost, treatment and co-morbidities in an employed population.

Wu EQ, Birnbaum H, Mareva M, Parece A, Huang Z, Mallett D, Taitel H
Pharmacoeconomics 2006;24(1):55-65

INTRODUCTION: Recent literature indicates that interstitial cystitis (IC) may affect 20% of women and a smaller proportion of men, although many individuals with IC may be misdiagnosed or remain undiagnosed. Factors that can contribute to the cost of IC include medical and drug utilisation related to treatment and diagnosis of IC and associated conditions (e.g. depression), as well as employee work loss. This study assesses the direct medical cost and indirect cost of work loss for IC patients in the first year after diagnosis, and evaluates IC treatment patterns and prevalence of co-morbidities. **METHODS:** Data for patients under the age of 65 years with at least one diagnosis of IC (n = 749) were drawn from a de-identified, administrative database of approximately 2 million beneficiaries that included medical, drug and disability claims for 1999-2002. A 2 : 1 matched control sample of patients without an IC diagnosis

(non-IC sample) was randomly selected based on patient characteristics. Indirect costs were calculated from a subgroup of 152 IC patients (plus their matched controls) who had disability information available. Costs incurred in the first year after IC diagnosis and co-morbidities were compared between IC patients and the non-IC sample, with the difference in costs defined as 'excess costs' of IC patients. Treatment patterns were profiled in the 2 months following initial diagnosis of IC. Descriptive statistics are presented. A multivariate two-part model was applied to estimate the IC direct medical cost, indirect cost and total cost to adjust for observed patient demographics and co-morbidities. Statistical significance was evaluated by the bootstrap method. RESULTS: The average IC patient had 130% higher direct costs ($p < 0.05$) and the average IC employee patient had 84% higher indirect costs than the average non-IC control individual. **IC patients also had a higher diagnostic prevalence of prostatitis (relative risk [RR] = 40.0), endometriosis (RR = 7.4), vulvodynia (RR = 6.9), chronic pelvic pain (RR = 5.8) and urinary tract infections (RR = 5.1) [all $p < 0.05$].** IC patients were also more likely to report depression (RR = 2.8) and anxiety (RR = 4.5) than non-IC controls (all $p < 0.05$). Seventeen percent of IC patients received pentosan polysulfate therapy, the only US FDA-approved oral drug therapy indicated for treating IC, within the first 2 months after diagnosis. Of these patients, 69% received at least one 'other' drug from the non-approved oral medications studied. Approximately one-third of IC patients received only 'other' drug therapies, and almost half of IC patients received no drug treatment within the first 2 months after the initial diagnosis. CONCLUSIONS: IC is a costly disease associated with co-morbidities. Following diagnosis, patients with IC are commonly untreated or treated with non-approved drug therapies. It is possible that more accurate diagnosis and earlier and more appropriate treatment of IC would lead to better management (or even prevention) of co-morbidities and reduce healthcare costs, and this should be investigated in future studies.

Vulvar vestibulitis syndrome: an important factor in the evaluation of lifelong vaginismus?

Ter Kuile MM, Van Lankveld JJ, Vlieland CV, Willekes C, Weijnenborg PT
J Psychosom Obstet Gynaecol 2005 Dec;26(4):245-9

The aim of the study was to investigate the prevalence of vulvar vestibulitis syndrome (VVS) in a sample of women suffering from lifelong vaginismus (N=91). Lifelong vaginismus is defined as "having a history of never having been able to experience penile entry of the vagina". The results with respect to VVS are compared with the results of women who are suffering from pain during intercourse (superficial dyspareunia) (N=84). Both patients groups were recruited from two treatment outcome studies. Using a standard physical examination, erythema was found in 77%, pain "on touch" in 69% and erythema and pain on the same location was seen in 56% of the patients with lifelong vaginismus. Furthermore, it was found that erythema (94%), pain (98%) and erythema and pain on the same location (92%) were more frequently found in patients with dyspareunia compared to women with lifelong vaginismus. It is concluded that pain is an integral part of the experiences in the majority of women with lifelong vaginismus.

Surgical treatment for the vulvar vestibulitis syndrome.

Traas MA, Bekkers RL, Dony JM, Blom M, van Haren AW, Hendriks JC, Vierhout ME
Obstet Gynecol 2006 Feb;107(2 Pt 1):256-62

OBJECTIVE: To study the outcome and complications of surgical treatment for vulvar vestibulitis syndrome and to identify patient characteristics that may have influenced the outcome. METHODS: Relevant patient characteristics were extracted retrospectively from the medical records of 155 women aged 40 years or younger who had received surgical treatment for vulvar vestibulitis syndrome. To assess outcome and complications, 126 of these 155 women (81%) participated in a telephone interview, conducted 1 to 4 years after surgery. RESULTS: After surgery 93% of the patients could have sexual intercourse compared with 78% before surgery; this increase was statistically significant (Mantel-Haenszel odds ratio 3.43, 95% confidence interval [CI] 1.48-7.96). In 62% of the women (95% CI 53-70%), sexual intercourse was painless after surgery. Eighty-nine percent (95% CI 84-95%) would recommend surgical treatment to other women experiencing vulvar vestibulitis syndrome. There were no major complications. Decreased lubrication during sexual arousal was the most frequently reported

adverse effect (24%, 95% CI 16-32%), followed by the development of a Bartholin's cyst (6%, 95% CI 2-10%). More of the women aged 30 years or younger reported that they could have sexual intercourse after surgery, and more of them would recommend surgical treatment to other patients than women aged 31 years or older. **CONCLUSION:** Surgical treatment for vulvar vestibulitis syndrome achieved high success rates with an acceptable rate of complications. Age of 30 years or younger was associated with a better outcome. **LEVEL OF EVIDENCE:** III.

Chronic pelvic pain treated with gabapentin and amitriptyline: a randomized controlled pilot study.

Sator-Katzenschlager SM, Scharbert G, Kress HG, Frickey N, Ellend A, Gleiss A, Kozek-Langenecker SA
Wien Klin Wochenschr 2005 Nov;111(21-22):761-8

BACKGROUND: The aim of this study was to compare the efficacy and side effects of gabapentin, amitriptyline, and their combination in women with chronic pelvic pain. **METHODS:** In this open-label, prospective, randomized trial, 56 women with chronic pelvic pain were investigated with a two-year follow-up at the Vienna Medical University Hospital. If pain intensity assessed by a visual analog scale (VAS) was 5 or more (0, no pain; 10, maximal pain), despite analgesic therapy using the nonopioid drug metamizol together with weak opioids, patients were randomized to receive gabapentin (n = 20), amitriptyline (n = 20), or a combination of both drugs (n = 16). Doses of gabapentin and amitriptyline were increased to maximum daily doses of 3600 mg and 150 mg, respectively, until sufficient pain relief or the occurrence of side effects. VAS and side effects were evaluated before treatment and at 1, 3, 6, 12 and 24 months afterwards. **RESULTS:** All patients experienced significant pain relief during the observation period. However, after 6, 12 and 24 months, pain relief was significantly better in patients receiving gabapentin either alone or in combination with amitriptyline than in patients receiving monotherapy with amitriptyline (gabapentin: 0 months, 7.7 +/- 1.5; 6 months, 1.6 +/- 0.9; 12 months, 1.5 +/- 0.9; 24 months, 1.9 +/- 0.9; amitriptyline: 0 months, 7.3 +/- 1.5; 6 months, 2.2 +/- 1.6; 12 months, 2.2 +/- 1.6; 24 months; 3.4 +/- 0.9; amitriptyline-gabapentin: 0 months, 7.6 +/- 0.8; 6 months, 1.3 +/- 0.9; 12 months, 1.7 +/- 1.0; 24 months, 2.3 +/- 0.9). Side effects were lower in the gabapentin group than in the two other groups, the difference reaching statistical significance after three months (P < 0.05). **CONCLUSION:** Gabapentin alone or in combination with amitriptyline is better than amitriptyline alone in the treatment of female chronic pelvic pain.

Prevalence and correlates of depression in treatment-seeking women with vulvodynia.

Masheb RM, Wang E, Lozano C, Kerns RD
J Obstet Gynaecol 2005 Nov;25(8):786-913

This study aimed to examine rates and correlates of depression in a treatment-seeking sample of women with vulvodynia. A total of 53 women were independently diagnosed with vulvodynia and assessed with state-of-the-art measures of major depressive disorder (MDD) and depressive symptom severity as well as psychometrically established measures of pain severity, general functioning, sexual function and quality of life. Current and lifetime prevalence rates for MDD were 17% (n = 9) and 45% (n = 24), respectively. Women with current MDD reported significantly greater pain severity, and worse functioning and quality of life than women without current MDD. Among those with lifetime MDD, the majority (62.5%) reported that their first depressive episode occurred before the onset of vulvodynia. Rates of current MDD appeared to be lower than rates of MDD among other samples of treatment seeking chronic pain patients. In summary, co-morbid MDD is related to greater pain severity and worse functioning among women with vulvodynia.

Silent pain sufferers.

Watkins E, Wollan PC, Melton III LJ, Yawn BP
Mayo Clin Proc. 2006;81(2):167-171

OBJECTIVE: To evaluate the proportion and characteristics of patients with chronic pain who do not seek treatment and assess whether these patients have unmet pain care needs. **PATIENTS AND METHODS:**

We performed a cross-sectional survey of residents of Olmsted County, Minnesota, from March through June 2004, with additional visit and diagnosis data from the Rochester Epidemiology Project database. Study participants were a random, population-based sample of eligible adult (>30 years) residents of Olmsted County with at least 1 visit to a local health care facility in the past 3 years. RESULTS: Of the 5897 eligible participants, 3575 people (60.6%) responded. Of the respondents who reported pain of more than 3 months' duration, 497 (22.4%) of the 2211 patients stated that they had not informed their physician about their pain. Of these silent sufferers, 70.6% (351/497) reported having moderate or severe pain, 49.2% (243/497) reported having frequent pain (>8 days per month), and 40.6% (202/497) met both criteria. Silent sufferers also reported that pain interfered with their general activity and sleep to a level only slightly less than the chronic pain sufferers who reported discussing their pain with a physician. Silent sufferers made an average of 5.2 ambulatory physician visits per year, which was less than those who sought physician help for their pain (8.6 ambulatory visits per year; $P<.001$). Men and younger participants were more likely to be silent about their pain ($P<.001$). CONCLUSION: More than 1 in 5 people with chronic pain did not seek physician care for their pain. This group is unknown to physicians and therefore represents an unreported patient group with an unmet need for pain care.

Vulvar Dermatoses

None.

Infectious Disease

Throwing the dice for the diagnosis of vaginal complaints?

Schwartz A, Taras D, Rusch K, Rusch V

Ann Clin Microbiol Antimicrob 2006 Feb 17;15(1):4 [Epub ahead of print]

ABSTRACT: Background: Vaginitis is among the most common conditions women are seeking medical care for. Although these infections can easily be treated, the relapse rate is high. This may be due to inadequate use of the diagnostic potential. METHODS: We evaluated the misjudgement rate of the aetiology of vaginal complaints. A total of 220 vaginal samples from women with a vaginal complaint were obtained and analysed for numbers of total lactobacilli, H₂O₂-producing lactobacilli, total aerobic cell counts and total anaerobic cell counts including bifidobacteria, Bacteroides spp., Prevotella spp. Additionally, the presence of Atopobium vaginae, Gardnerella vaginalis, Candida spp. and Trichomonas vaginalis was evaluated by DNA-hybridisation using the PCR and Affirm VPIII Microbial Identification Test, respectively. RESULTS: The participating physicians diagnosed bacterial vaginosis (BV) as origin of discomfort in 80 cases, candidiasis in 109 cases and mixed infections in 8 cases. However, a present BV, defined as lack of H₂O₂-lactobacilli, presence of marker organisms, such as G. vaginalis, Bacteroides spp. or Atopobium vaginae, and an elevated pH were identified in only 45 cases of the women examined. Candida spp. were detected in 46 cases. Interestingly, an elevated pH corresponded solely to the presence of Atopobium vaginae, which was detected in 11 cases. CONCLUSION: Errors in the diagnosis of BV and candida vulvovaginitis (CV) were high. Interestingly, the cases of misjudgement of CV (77%) were more numerous than that of BV (61%). The use of Amsel criteria or microscopy did not reduce the number of misinterpretations. The study reveals that the misdiagnosis of vaginal complaints is rather high.

An evaluation of butoconazole nitrate 2% site release vaginal cream (Gynazole-1) compared to fluconazole 150 mg tablets (Diflucan) in the time to relief of symptoms in patients with vulvovaginal candidiasis.

Seidman LS, Skokos CK

Infect Dis Obstet Gynecol 2005 Dec;13(4):197-206

BACKGROUND: It is estimated that as many as 13 million cases of vulvovaginal infection occur in the

United States annually, the majority of which are the result of *Candida albicans* infection. The symptoms of vulvovaginal infections are often painful and distressing to the patient. The objective of this study was to compare the time to symptomatic relief of vulvovaginal candidiasis (VVC) with butoconazole nitrate 2% Site Release vaginal cream (Gynazole-1) and oral fluconazole 150 mg tablets (Diflucan). METHODS: This randomized, open-label, parallel study evaluated 181 female patients with moderate to severe symptoms of VVC. Patients were randomized to single-dose therapy with either butoconazole nitrate 2% Site Release vaginal cream or fluconazole. The primary outcome measure was the time to onset of first relief of symptoms. Secondary measures included the time to overall relief of symptoms and the reinfection rate over the first 30 days following treatment. The overall safety of both products was investigated through the collection of adverse event reports. RESULTS: The median time to first relief of symptoms occurred at 17.5 h for butoconazole patients as compared to 22.9 h for fluconazole patients ($p < 0.001$). The time at which 75% of patients experienced first relief of symptoms was 24.5 h versus 46.3 h for butoconazole and fluconazole, respectively ($p < 0.001$). By 12- and 24-h post-treatment, 44.4% and 72.8% of patients in the butoconazole treatment group reported first relief of symptoms versus 29.1% and 55.7% of patients in the fluconazole group ($p = 0.044$ and $p = 0.024$ respectively). In patients experiencing first relief of symptoms within 48 h of dosing, the median time to first relief of symptoms in the butoconazole treatment group was significantly shorter at 12.9 h compared to 20.7 h for the fluconazole treatment group ($p = 0.048$). There were no significant differences between the two groups with respect to time to total relief of symptoms or reoccurrence of infection within 30 days of treatment. Butoconazole therapy was shown to have fewer reported adverse events, including drug-related adverse events, than fluconazole therapy. Vulvovaginal pruritis and vulvovaginal burning were the most common drug-related adverse events attributed to butoconazole. Headache, diarrhea, nausea, upset stomach and skin sensitivity were the most common drug-related adverse events attributable to fluconazole. CONCLUSIONS: Single-dose butoconazole nitrate 2% Site Release vaginal cream provides statistically significant improvement in time to first relief of symptoms in the treatment of VVC compared to fluconazole. There is no difference between these two treatments with respect to total relief of symptoms or reinfection rate. Although there was no significant difference in the incidence of adverse events judged by the investigator to be treatment-related, butoconazole treatment did result in fewer patients experiencing adverse events than fluconazole.

Basic Science

None.