

The Future of Vulvar Disease: Ongoing and New Challenges

C Marchitelli, MD¹. ¹Chief of Vulvar Department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

The International Society for the Study of Vulvovaginal Disease works diligently to promote teamwork and to collaborate among nationalities and medical disciplines.

Our challenges:

Teamwork: Today’s society rewards individual work for personal benefits. To work as a team, we often must ignore our individual desires. We believe, “If you want to go fast, go alone; if you want to go far, go together”. Goals are more easily achieved if we work together.

Become mentors: We believe by sharing our information and our experience by being generous and trying to pass on to others everything we have learned we truly impact the future. If we keep knowledge to ourselves it loses its essence. It becomes pointless. By being a mentor, you can leave a permanent mark on another person’s life.

Spread the knowledge all around the world, especially to underdeveloped countries. It can be challenging, but we must reach out to those that cannot afford to pay for expensive meetings and annual fees to become members of Societies.

We must improve clinical trials on most vulvar diseases. Throughout healthcare fields, clinical trial and observational studies, investigators have recognized the need for development of standard (core) outcomes and instruments to measure them. Core outcome sets/measures are key to the improvement of observational research and clinical trial methods. We will work together on this project.

New approaches to vulvovaginal diseases: Genomics and molecular biology will help us in describing pathogenesis and finding new treatments.

Recognize the importance of the whole woman: Women with vulvovaginal diseases carry a heavy burden that affects their family, social and sexual life. We are not treating a “vulva” we are treating a whole woman. We work for them NOT FOR US.

We all have a challenge, a scientific and a human challenge. To succeed we do not have to lose sight of whom we are working for.

Our mission is to take care of our patients!

Highlights on Clinical Research Regulations: Focus on ICH-GCP and Ethics

D Salmun, MD¹. ¹Clinical Trials Reviewer, ANMAT- Ministry of Health, Buenos Aires, Argentina.

Research means a systematic investigation, designed to develop or contribute to generalizable knowledge and is increasingly playing a role in various medical disciplines.

It is essential that a clinical research practice be based on ethics principles. An investigator in a clinical trial needs to know about the paramount importance to minimize risks of the people who consent to take part of it, as well as being aware of the relevant national and international laws and regulations.

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) is a unique arrangement bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

Directives for Good Clinical Practice (GCP) are recorded in the ICH-GCP Guideline E6. The ICH-GCP are defined as “*international ethics and quality standards for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.*” Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and the clinical trial data are credible (www.ich.org).

In November 2016, the second revision to ICH - GCP E6 (R2), the largest revision to GCP in 20 years, was published.

For the last 50 years, the protection from harm caused by the conduct of research studies and protection of the persons who consent to participate has become crucial for researchers, ethicists and the totality of stakeholders involved in clinical research worldwide. Current laws and regulations aim at such protection by ensuring Good Clinical Practice.

Update on Chronic Recurrent Vulvovaginitis

G Donders¹. ¹Femicare Clinical Research for Women Tienen & University Hospital, Antwerp, Belgium.

Recurrent vulvovaginitis (RVV) is one of the most frequent reasons for a woman to visit a gynecologist. The burden of such infections is high for both patients and health care workers. Despite its frequency, little effect has been achieved over the years to prevent RVV. Dietary measures and behavioral adaptation have failed to decrease recurrent bacterial vaginosis (RBV), recurrent candida vaginitis (RCV), or recurrent aerobic vaginitis (RAV). Reinfection does not seem to be the major cause of the recurrences, rather endogenous, immunogenetic tolerance seems too crucial to maintain the abnormal microbiome in these conditions. Furthermore, in recurrent Trichomonas vaginitis (RTV), where reinfection does play an important role in most cases, resistance to currently used antibiotics has emerged. Vaccination trials have not been sufficiently successful to justify promising patients a clinical useful vaccine, anytime soon, for any of these infections. Concerning treatment, we are aware that the current standard treatment of BV with metronidazole or clindamycin is far from ideal and does not cure more than 2/3 of the relapses. Recently, new disinfectants and antibiotics were shown to have at least equal efficacy compared to standard drugs, opening the possibility to vary and combine treatments for women with RBV. For RCV, most newly introduced triazoles do not have a profile sufficiently different from the existent drugs to promise large improvements in recurrence prevention. Instead a continuous, individualized regressive regimen with fluconazole (ReCiDiF) is the most widely used treatment program in Europe and abroad, keeping women relapse free in 90% and 78% after 6 months and a year, respectively. Non-responders have a higher likelihood to have an atopic constitution, or have switched to a different genotype of *Candida albicans* or even to a non-*albicans* infection. For these women, switching to non-azole treatments is advised (boric acid, amphotericin B or flucytosine). These patients are often managed in specialized centers. Glucose or yeast lowering diets, as well as several other behavioral changes, are seldom helpful and should only be maintained if they were proven to reduce recurrences. For RAV several antibiotics such as local kanamycin or moxifloxacin can help for a short while, but tailored treatment according to the microscopic findings of the level of atrophy, number and type of microorganisms and inflammation give the best long-term results and satisfaction for patients. Theoretically, based on antimicrobial properties in lab circumstances, different probiotics are pushed forward as ideal, natural and efficient ways to treat and prevent recurrences of RVV. A word of caution: most products, both for oral and vaginal use, are widely promoted despite a lack of clinical evidence of efficacy. We advocate using only those products that can submit proper clinical effects on delineated indications.

Approaching Vulvovaginal Candidiasis: Developing Drugs for Treatment – FDA Draft Guidance for Industry

D Salmun, MD¹. ¹Clinical Trials Reviewer, ANMAT- Ministry of Health, Buenos Aires, Argentina.

The Food and Drug Administration (FDA) announced the availability of a draft guidance for industry entitled “*Vulvovaginal Candidiasis: Developing Drugs for Treatment.*” The comments on this draft guidance were submitted to the Agency until September 29, 2016.

This guideline, prepared by the FDA Center for Drug Evaluation and Research (CDER) - Division for Anti-Infective Drug Products-, supersedes 1998 FDA draft guidance: “Vulvovaginal Candidiasis: Developing Antimicrobial Drugs for Treatment.”

In a Federal Register notice dated August 7, 2013, FDA announced that such 1998 draft guidance was being withdrawn as new information, scientific developments, and emerging technologies require a revision.

The purpose of the guidance we are approaching is to assist sponsors in the overall clinical development program and clinical trial designs to support drugs being developed for the treatment of VVC. In addition, it reflects recent developments in scientific information that pertain to such drugs.

In general, this guidance focuses only on developing antifungal drugs (discovery and clinical research) for the treatment of uncomplicated vulvovaginal candidiasis (VVC), generally defined as a single episode of vulvovaginal inflammation caused by *Candida* yeast in an otherwise healthy female. For complicated VVC the dose, duration, or formulation of antifungal treatment may be

different in comparison to uncomplicated VVC, thus they are not discussed in this document.

This document helps define enrollment criteria for VVC trials, and recommends that such trials be superiority trials against placebo or active control. The recommended efficacy endpoint is resolution of clinical signs and symptoms.

Remarkably, this guidance does not discuss trial designs for development programs for nonprescription treatments of VVC. Neither does this contain a discussion on general issues in drug development or general issues of statistical analysis or clinical trial design.

Update-2 Management of Ulcers - Consensus

N Madhani, MD¹. ¹Dermatology Consultant, P.D. Hinduja National Hospital & MRC, Mumbai, India.

Vulvar ulcers are painful, debilitating, and severely compromise the quality of life (QoL) of the individual. Etiology is varied ranging from infections (herpes simplex, herpes zoster, impetigo, candidiasis), inflammatory (erosive lichen planus, lichen sclerosis, irritant contact dermatitis), blistering disorders (pemphigus, bullous pemphigoid, linear IgA, cicatricial pemphigoid, Hailey-Hailey disease) and premalignancies (high grade vulvar intraepithelial lesion (HSIL) of the vulva), and malignancies (squamous carcinomas, basal cell carcinomas, extra-mammary Paget's disease, and Langerhans cell histiocytosis). Clinical features are often overlapping, and diagnosis depends on exhaustive history taking, and histopathology. Except for the management of infections, where clinical, diagnostic, and therapy guidelines have been laid out; other diseases suffer from a paucity of randomized studies, and small sample sizes, with no definite consensus criteria. An attempt is made to lay down recommendations for diagnosing and managing vulvar ulcers, by collating data from existing publications, from the Medline (PubMed) database.

Vulvodynia Update

L Sadownik¹. ¹Director, BC Centre for Vulvar Health, Associate Professor, Department of Gynecology, Associate Member, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada.

The objectives of this update are to: (1) selectively review the published literature on vulvodynia; (2) highlight specific advances in knowledge; and (3) speculate on how this knowledge may translate into advances in clinical management and/or research. A search was made in Medline/PubMed (time period 2015-2017) using the words vulvodynia/vestibulodynia and the following terms etiology, epidemiology, diagnosis, and treatment/management and research. Select articles were chosen for presentation and discussion. This update will review the currently accepted terminology and classification of persistent vulvar pain and vulvodynia. Current practice patterns will be analyzed by reviewing the recommendations of experts regarding the management of vulvodynia; and then comparing these to evidence regarding practice patterns for the management of vulvodynia in the United States. Topical medications are a popular intervention for vulvodynia and recent research has identified specific inflammatory responses in the vestibular mucosa that may contribute to the onset or amplification of vulvar pain. Treatment studies report a positive effect of medical (topical steroid), psychological (Cognitive Behavioral Therapy), and physical therapeutic interventions on reducing pain. Analysis of the research methodology in the field demonstrates that researchers are reporting on a broader range of treatment outcomes that: measure the bio psychosocial health of women with vulvodynia; and reflect the six core outcome domains for chronic pain clinical trials recommended by the Initiative on Methods, Measurement and Pain Assessment in Clinic Trials (IMMPACT). The Vulvar Pain Assessment Questionnaire Inventory (VPAQ) is an example of a multidimensional assessment tool specifically developed for vulvodynia. A comprehensive definition of treatment success may provide guidance to health care providers and patients regarding vulvodynia therapies.

Quality of Life After Surgery vs. Conservative Treatment for Local Provoked Vulvodynia

A Aalto, MD^{1,2}, H Huhtala, MSc³, J Mäenpää, MD, PhD^{1,4}, and S Staff, MD, PhD^{1,4}. ¹School of Medicine, Tampere University, Tampere, Finland. ²Department of Obstetrics and Gynecology, Kanta-Häme Central Hospital, Hämeenlinna, Finland. ³Faculty of Social Sciences, University of Tampere, Tampere, Finland. ⁴Department of Obstetrics and Gynecology, Tampere University Hospital, Tampere, Finland.

Objectives: Surgical removal of painful tissue (posterior vestibulectomy) is considered the last treatment option for local, provoked vulvodynia (LPV) if conservative treatments fail to reduce the pain sufficiently. The aim of our study was to compare quality of life (QoL) of LPV patients (surgery vs. conservative treatment) with validated questionnaire. QoL data obtained from LPV patients was also compared to population-based QoL data obtained from healthy age-matched women.

Methods: Our study consisted of a retrospective patient cohort of surgically (n = 13) treated LPV patients and conservatively treated controls (n = 23). Data were collected by review of patient records and postal questionnaires. A Finnish validated version of RAND-36 questionnaire was used for QoL measurement.

Results: QoL between surgeries vs. conservative treatment groups did not differ significantly. However, conservatively treated LPV patients had a statistically significant lower quality of life than healthy women in general health (62.1 SD 23.9 vs. 74.9 SD 17.8 p = 0.018), emotional role functioning (56.5 SD 43.9 vs. 76.7 SD 34.0 p = 0.049), and pain dimension (64.7 SD 24.5 vs. 80.5 SD 21.2 p = 0.005).

Conclusions: Patients treated conservatively for LPV suffer from poorer quality of life than healthy women at same age in general health, emotional role functioning and pain dimension. This study suggests that surgery may be superior to conservative treatment in LPV with respect to quality of life.

Mindfulness-Based Group Cognitive Behavior Therapy for Women with Provoked Localized Vulvodynia: A Randomized Controlled Trial

A Guillet, MD^{1,3}, N Cirino, MD^{2,3}, C Polan-Orzech, MA, LMFT^{2,3}, and C Leclair, MD^{1,3}. ¹Department of Obstetrics and Gynecology, Health, Oregon Health Sciences University, Portland, OR, USA. ²Department of Psychiatry, Health, Oregon Health Sciences University, Portland, OR, USA. ³Center for Women's Health, Oregon Health Sciences University, Portland, OR, USA.

Objectives: The purpose of this study is to evaluate the effectiveness of mindfulness-based group cognitive behavior therapy (M-gCBT) compared to education-support group therapy alone for the treatment of the pain and distress associated with provoked localized vulvodynia (PLV).

Methods: A randomized controlled trial was conducted using two cohorts of participants for a total of thirty-one participants randomized to M-gCBT or education-support group therapy. Pre-study questionnaires were administered and the cohorts subsequently underwent an 8-week long program. M-gCBT participants attended weekly sessions. Participants in the education-support group had 8 weeks of online-education with 3 in-person support visits. Vaginal insertion pain (Tampon Test) was the primary outcome. Sexual function and quality of life were also evaluated. Questionnaires were administered at the completion of the study period, at 3 months, and at 6 months.

Results: A total of 32 participations were enrolled and 31 were randomized. There were 14 participants who were randomized and completed M-gCBT and 17 that were randomized and completed education-support group therapy. Baseline characteristics did not differ significantly with respect to baseline tampon test, BMI, relationship status, age of menarche, use of hormonal contraception, or previous pregnancy. Age was significantly different between the two groups. On average, vaginal insertion pain measured by the Tampon Test decreased at the end of study though was not significantly different between the two groups (p = 0.764). The Female Sexual Function Index (FSFI) and Female Sexual Distress Score (FSDS) showed improvement in both groups at the end of the study, though it was significantly more improved in the M-gCBT group (p = 0.013 and p = 0.005, respectively). All sexual function and quality of life measures trended towards improvement in both groups.

Conclusions: Based on the results of this RCT, both m-gCBT and education-support can be effective in reducing pain and sexual distress associated with PLV. However, an 8-week long m-gCBT program may be more effective at reducing sexual distress in particular. Women expressed a high amount of satisfaction, which was reflected in the statistically significant improvement in quality of life and sexual function outcome scores. Longer term data are currently being collected.

Acupuncture Augmentation of Lidocaine Treatment for Provoked Localized Vulvodynia – A Pilot Study

LE Hullender Rubin, DAOM^{1,2}, SD Mist, PhD³, RN Schnyer, DAOM⁴, and CM Leclair, MD¹. ¹Department of Obstetrics and Gynecology, Oregon Health and Science University, Portland, OR, USA. ²Research Department, Oregon College of Oriental Medicine, Portland, OR, USA. ³Department of Nursing, Oregon Health and Science University, Portland, OR, USA. ⁴Department of Nursing, University of Texas, Austin, TX, USA.

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Objectives: To assess acupuncture's augmentation of lidocaine therapy in the treatment of provoked localized vulvodynia (PLV).

Methods: In a randomized, single blind controlled trial over 12 weeks, 19 women with moderate to severe PLV were randomized to either 18 sessions each of classical acupuncture (CA) or non-classical acupuncture (NCA). Women in the CA group received alternating sessions of manual or electro-acupuncture. The NCA group received minimal needling with no stimulation. All participants applied lidocaine 5% cream four times daily to the vestibule. The primary outcome was change in Tampon Test scores using a 100-point visual analogue scale (VAS) from baseline and week 12.

Results: Participants in both groups reported significant pain reduction over 12 weeks. Follow up scores were obtained in 14 women at week 24; 5 women withdrew from the study. Women in the CA group (n = 7) experienced a within group mean difference (MD) of 42.419.4 from baseline and 12 weeks (p = 0.001), and was maintained at week 24 (MD 35.717.8, p = 0.002). In the NCA group (n = 7), women experienced a within group MD 28.728.5 at 12 weeks (p = 0.04), and further improved at week 24 (MD 36.717.7, p = 0.002). There was no difference between groups.

Conclusions: In this early-phase research, acupuncture augmentation of lidocaine was acceptable and may reduce vestibular pain in women with PLV more than lidocaine alone. Both acupuncture techniques showed a favorable effect.

A Comparison of the Lidocaine Test to the Vulvagesiometer for the Diagnosis of Localized Provoked Vulvodynia (LPV)

A Stenson, MD, MPH¹, M Goetsch, MD¹, and C Leclair, MD¹. ¹Program in Vulvar Health, Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland, OR, USA.

Objectives: The purpose of this study was to compare the lidocaine test (LT) to the vulvagesiometer (VG) for diagnosing patients with localized provoked vulvodynia (LPV).

Methods: Reproductive-age women with LPV were evaluated by cotton swab test (CST) at 6 sites and VG at 2 sites with the order of initial test randomized. Participants reported pain using a numeric rating scale 0-10 (NRS). For the VG, up to 6 pressures were tested as tolerated (10, 25, 50, 100, 200 and 300 grams). Lidocaine 4% topical solution was then applied for three minutes and the CST and VG repeated in order of randomization. Demographics were analyzed using t-tests and Fisher's exact tests. Changes in NRS with lidocaine application were analyzed using paired t-tests. Pain threshold pressure (NRS > 4) and max tolerated pressure differences (pre-and post lidocaine) were analyzed using Wilcoxon signed rank tests. The relationship between the CST and VG was analyzed by computing Spearman's correlation coefficients.

Results: 16 patients completed the study, 8 in each arm (CST or VG first). Lidocaine significantly reduced pain with the CST and VG at all pressure points (P < 0.05). Max tolerated pressure with application of lidocaine increased significantly (p < 0.005). After lidocaine application, most participants reported pain (NRS > 4) at pressures of 100-200grams.

Conclusions: Lidocaine application extinguishes mucosal vestibular tenderness provoked by both diagnostic tools. Pressures above 100-200 grams may evoke pain other than mucosal allodynia of LPV since lidocaine was less able to extinguish pain at these pressure levels.

Lower Urinary Tract Symptoms in a Chronic Pain Population

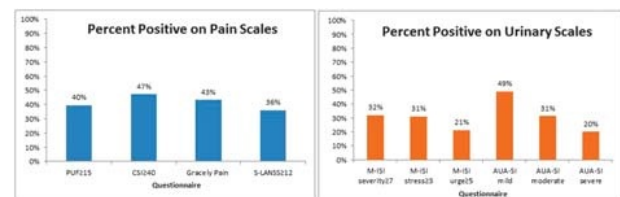
AG Sammarco, MD, MPH¹, EK Kobernik, MPH, CPH¹, HK Haefner, MD¹, and MB Berger, MD, PhD¹. ¹Michigan Medicine, Department of Obstetrics and Gynecology, Ann Arbor, MI, USA.

Objectives: To characterize the prevalence of lower urinary tract symptoms (LUTS) in a chronic pain population.

Methods: Patients referred to a female pelvic pain clinic at our institution completed several validated questionnaires regarding pain and bladder symptoms including the pelvic pain and urgency/frequency patient symptom scale (PUF), central sensitization inventory (CSI), the American Urological Association symptom index (AUA-SI) and the Michigan incontinence symptom index (M-ISI). Patients were excluded for interstitial cystitis/bladder pain syndrome. Survey responses were analyzed via Pearson's correlation coefficients and logistic regression.

Results: A total of 144 patients were included in the final analysis. Baseline scores are shown in figures 1a and 1b. Between 39 and 47% of patients screened positive on the PUF and CSI questionnaires. AUA-SI data showed 48.8% of patients had mild, 31.2% had moderate and 20% had severe symptoms. M-ISI data showed 31.9% had a severity score ≥ 7 , 31% had a stress incontinence score ≥ 3 and 21% had an urgency incontinence score ≥ 5 . The CSI and PUF were moderately correlated with AUA-SI total scores (PUF $r = .54$, $p < .0001$, CSI $r = .65$, $p < .0001$). Logistic regression models demonstrated that the CSI and PUF are both significantly associated with having moderate to severe symptoms on AUA-SI, and that a diagnosis of vestibulodynia had a protective effect (Table 1).

Conclusions: There is a high prevalence of LUTS among patients with chronic pelvic pain. Vestibulodynia was associated with a lower likelihood of bladder symptoms and high PUF and CSI scores were significantly associated with moderate to severe bladder symptoms.



PUF: Pelvic Pain and Urgency/Frequency patient symptom scale
CSI: Central Sensitization Inventory
Gracely Pain: Gracely Pain Intensity Scale – pain outside of intercourse
S-LANSS: Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs
AUA-SI: American Urological Association Symptom Index
M-ISI: Michigan Incontinence Symptom Index (M-ISI)

Predictors of Moderate-Severe symptoms on AUA-SI

	Unadjusted Odds Ratio	Adjusted Odds Ratio	95% Confidence Interval	p
Age	1.02	1.02	(0.99-1.05)	0.31
BMI	1.01	1.01	(0.95-1.08)	0.76
Vestibular Pain	0.35	0.28	(0.11-0.74)	0.01
PUF	7.58	4.4	(1.58-12.2)	0.005
CSI	5.99	4.39	(1.67-11.52)	0.003

BMI: Body Mass Index
PUF: Pelvic Pain and Urgency/Frequency patient symptom scale
CSI: Central Sensitization Inventory

These included the Pelvic Pain and Urgency/Frequency patient symptom scale (PUF), the Central Sensitization Inventory (CSI), the Gracely Pain Intensity Scale, the Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS), the PROMIS Anxiety 7a and Depression 8a forms, the McGill Pain Questionnaire, the Gracely pain questionnaire, a visual analog scale (VAS), the American Urological Association Symptom Index (AUA-SI) and the Michigan Incontinence Symptom Index (M-ISI).

Physiotherapeutic Treatment in Vulvodynia

L Mompó¹, MI Marti¹, RA Domenech¹, and LM Grajales¹. ¹Area of Pelvic Floor Reeducation, Physiotherapy area, Gynecology area, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: Highlight an interdisciplinary physiotherapeutic approach for the treatment of patients with vulvodynia.

Methods: From 2010 to 2016, 259 patients were assisted with generalized and localized vulvodynia. The techniques for rehabilitation are: The initial evaluation is outlined in table 1.

Results: 259 patients completed 9 sessions; 66% received physiotherapy alone, and 34% received pharmacotherapy and physiotherapy. The mean age was 41 years (range:19-82). 83% reported substantial clinical improvement. 45% were asymptomatic after treatment. 38% reported moderate improvement.

TABLE 1. Illustrates the clinical record, physical examination techniques and treatment for this form of therapy for vulvodynia.

Clinical record, physical examination	Technique
External evaluation in order to observe the state of the skin and the presence of scars.	Visual
Internal evaluation to determine the vaginal opening, trigger points, muscle retractions, contraction capacity, and pelvic floor muscle tone	Manual techniques (aiming to desensitize the area and decrease pain, improve the circulation and normalize the muscle tone). Biofeedback to evaluate the capacity of muscle relaxation (muscle stretching technique). Therapeutic exercises (individualized to each patient to maintain and improve patient outcome; includes global exercises to mobilize the pelvis, abdomen and lower extremities). Auto massage and stretching of the pelvic floor muscles, especially the perineum.
Treatments	
Electrotherapy	Neuromodulation of the posterior tibial nerve.
Behavioral changes	Implemented at the beginning of the treatment (modify risk factors).

Conclusions: The interdisciplinary treatment demonstrates that physiotherapy represents a good alternative for the management of patients with vulvodynia.

Risk Factors for Vulvodynia: A Systematic Review

H Graetz¹, A White², and HC Frawley, PhD^{3,4}. ¹The Royal Hospital for Women, Sydney, Australia. ² Darlington Physiotherapy, Sydney, Australia. ³Monash University, Frankston, Victoria, Australia. ⁴ Cabrini Health, Malvern, Victoria, Australia.

Objectives: The objective was to systematically review the literature on the risk factors for vulvodynia.

Methods: A systematic review was conducted as per preferred reporting items for Systematic reviews and meta-analyses (PRISMA) guidelines. The search was undertaken for risk factors for vulvodynia; across PubMed, Ovid, ProQuest and Science Direct databases. The methodological quality was assessed by two independent reviewers using standardized criteria before analysis of main results.

Results: 18 observational studies covering 11 different cohorts, including 3 cohorts, 4 cross-sectional and 11 case control studies fulfilled inclusion criteria. Fifty-seven factors were assessed across three different domains: gynecological (19), medical (24), and psychosocial (14). Reported incidence of vulvodynia was between 3/100 and 11/100. Factors consistently identified as contributing to the risk of vulvodynia included oral contraceptive use (ever used, duration of use greater than 2–6 years and younger than 17 years of age at commencement of oral contraceptive pill); and combination or single reports of urogenital infection and comorbid pain conditions. Anxiety and a childhood experience of severe abuse were psychosocial factors highly linked with vulvodynia. The predictive ability and degree of risk was difficult to categorically determine because of confounders, heterogeneity of populations, and methodologies, and a lack of cohort studies.

Conclusions: Many gynecological, medical and psychosocial risk factors for vulvodynia have been demonstrated to exist. Recent investigations have widened the scope of etiological considerations for vulvodynia and with recently updated vulvar pain terminology. This review may assist in the identification of risk and guide efforts in the prevention of vulvodynia.

Vulvar and Clitoral Pain after Female Genital Mutilation/Cutting: Diagnosis and Treatments

J Abdulcadir¹, and P Petignat¹. ¹Geneva University Hospitals, University of Geneva, Geneva, Switzerland.

Objectives: Female genital mutilation/cutting (FGM/C) involves the partial or total removal of the female genitalia for non-therapeutic reasons. It can involve the cutting of the clitoris and cause psychological, sexual, and physical

complications. Pain from FGM/C originates from scarring complications. A recent literature review regarding management for clitoral/vulvar pain after FGM/C identified no studies. Our aim is to present the management of 6 cases of clitoral/vulvar pain after FGM/C.

Methods: This is a case study of 6 patients who presented to the specialized clinic for women with FGM/C of the Geneva University Hospitals. Multidisciplinary care is offered by a gynecologist; a sexual counselor; midwives trained in pelvic floor muscle training; a psychologist and a psychiatrist (both sex therapists).

Results: We present a series of complications after female genital mutilation/cutting a) 3 cases of painful clitoral cysts managed with surgical excision. Histopathology revealed a post-traumatic clitoral neuroma and granuloma, a Mullerian cyst, and a clitoral epidermoid cyst. Clitoral pain was resolved 1-year post-surgical revision. b) 2 cases of superficial dyspareunia after FGM/C type III managed with anterior, and anterior and posterior defibulation (opening of the vulva with reconstruction of the labia minora). c) 1 case of chronic and provoked clitoral pain without a mass, successfully managed through clitoral reconstructive surgery. Following excision of periclitoral fibrosis a clitoral neuroma was identified and excised. In this patient, post-traumatic stress disorder (due to recall of the FGM/C experience) manifested following surgery. Psychotherapy and medical treatment were successful with resolution of clitoral pain symptoms.

Conclusions: Despite the lack of evidence, there are successful treatments for pain after FGM/C.

Acute Idiopathic Ulcers: A Case Series and Review of the Literature

GD Saïke¹, CE Marchitelli², MC Sluga¹, MS Peremateu¹, MM Domenech¹, MJ Martinez³ and S Gogorza⁴. ¹Center of Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ²Chief of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ³Fellow of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁴Chief of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: To report our cases at the Italian Hospital of Buenos Aires over a 6-year time period.

Methods: Ten patients presented with acute vulvar ulcers that appeared in the context of a febrile syndrome. The ages ranged from 11 to 49 years. Adolescents under the age of 18 had not initiated sexual activity. A complete history, physical examination, and laboratory testing were carried out to rule out both venereal diseases and other usual causes of vulvar ulcers including: blood testing with serology for human immunodeficiency virus type 1 and 2, venereal disease research laboratory test (VDRL), toxoplasmosis, cytomegalovirus (CMV), herpes simplex types 1 and 2, and Epstein-Barr virus were performed. Mycoplasma culture of the lesions and polymerase chain reaction (PCR) for detection of viral DNA (herpes and EBV) were done. A biopsy was performed in only two cases.

Results: The lesions were unilateral in 1 case and bilateral in 9 cases. All patients presented with leukocytosis with a predominance of polymorphonuclear cells. In 4 patients, an increase in AC IG G anti-HSV type 1 and anti-VCA IgG (viral capsule antigen) EB was observed. In two patients,



serology was positive for CMV, and one for Mycoplasma. Serologies were negative in five patients. Cultures were negative in all patients. The ulcers healed spontaneously.

Conclusions: This rare entity usually occurs in women without prior sexual intercourse, in the context of an influenza-like illness. The diagnosis is made by exclusion. In recent studies, it has been associated with primary infection by EBV. Laboratory tests and histopathology are often nonspecific. We were able to demonstrate the relationship with the EBV in 4 cases. The clinical course is self-limited and resolves spontaneously with no sequelae.



Hidradenoma Papilliferum of the Vulva: Report of 19 Cases

ML Absi, MD¹, C Marchitelli, MD², MC Sluga, MD³, G Secco, MD³, M Martinez, MD⁴, A Wernicke, MD⁵, and S Gogorza, MD⁶. ¹Resident of Obstetrics and Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ²Chief of the Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ³Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁴Fellow of the Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁵Pathology service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁶Chief of gynecology section, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: To describe the main characteristics and treatment course of 19 cases of hidradenoma papilliferum of the vulva treated at the department of gynecology, Hospital Italiano of Buenos Aires, Argentina.

Methods: We reviewed 19 cases of hidradenoma papilliferum in women who were diagnosed between January 2008 and January 2016. The mean age was 47 years (27-78 years). The most frequent location was labia majora (9/19), followed by the interlabial sulci (6/19). The size of the tumors ranged between a few millimeters to 3-4 cm. Though the disease is generally asymptomatic (14/19), it may also present with pruritus (4/19), or pain (1/19).

Results: The diagnosis of hidradenoma papilliferum is confirmed by histology. The standard treatment is wide local excision secondary to the association with malignancy, although this occurs infrequently. All our patients were surgically treated, and simple excision was curative. There have not been any recurrences during follow-up.

Conclusions: Hidradenoma papilliferum is the most frequent glandular tumor of the vulva. They arise from the apocrine sweat glands but, since they often occur along the known distribution of mammary-like glands, some authors consider them to be the cutaneous counterpart of mammary intraductal papillomas. They

can be a challenge for health care providers because of their variable clinical presentation. Differential diagnoses are pyogenic granuloma, angioma, Bartholin cyst, or squamous cell carcinoma when ulceration is present. Rare cases of malignant changes have been reported; therefore, the simple excision is the recommended treatment.

A Retrospective Audit of Patients attending a New Community Multidisciplinary Vulva Clinic: The Invisible Vulva

G Edgley, MBBS, M App Sc¹, T Bohl, MBBS, Dip RACOG, FACD¹.
¹Vulva Clinic, Jean Hailes for Women's Health, Clayton, Victoria, Australia.

Objectives: Vulvovaginal complaints are common but poorly managed issues of sexual and reproductive health. We initiated a multidisciplinary vulva clinic based on a perceived need for improved community care. We performed an audit of the patients attending our clinic to establish an ongoing requirement for our services and to appropriately target education within our referral base to enhance the care of women in our community.

Methods: A retrospective review of the records of all the patients attending The Jean Hailes Vulva Clinic between July 1, 2015 and December 30, 2016 was made. Information was entered into a database and analyzed.

Results: 101 patients attended as new patients to the Jean Hailes Multidisciplinary Vulva Clinic over a period of eighteen months. The most common diagnosis was lichen sclerosus 50/101 (49.5%), either proven on biopsy or visual diagnosis; vulvar pain and/or dyspareunia 33/101, (32.7%) and candida 26/101 (25.7%). Within our population, we identified one patient with extra mammary Paget's disease and lichen sclerosus, one patient with high grade squamous intraepithelial lesions of the vulva (HSIL) and lichen sclerosus, and 2 patients with HSIL of the vulva. Common associations were lichen sclerosus and vulvar pain or dyspareunia (N = 7, 6.9%) and pain and candida. If a patient presented with pain, either vulvar pain or dyspareunia (N = 35, 34.6% patients) then 40% had candida albicans or candida glabrata as a cofactor. Vulvar pain, with no other associations was found in 7 patients (6.9%). Our patients were drawn from a 130 km radius to our clinic with a small percentage 3/101 (2.8%) from interstate and the majority travelling 50 kms or less. Patients had seen multiple practitioners prior to attending: mean 2.3 (range 0 to >5). Symptom duration varied from two months to ≥ 5 years (classified as long term). 45% of our new patients (N =46) had had symptoms for 5 or more years at presentation (range 2 months to 30 years).

Conclusions: Vulvovaginal complaints are a frequent reason for women to visit their primary care practitioner. We found that within a multidisciplinary vulva clinic placed within easy access to the community there were varied presentations and a high demand for services. Our patient profile confirmed previous findings that women's care was compromised by delayed and lengthy time to diagnosis. We found many varied diagnoses including 3 premalignant conditions and one malignancy. We demonstrated that there were several key diagnoses we could target within our referral base, with simple algorithms, to improve the outcomes for women in our catchment area.

Vulvar Endometriosis: A Series of 4 Cases

MF Marcos¹, C Marchitelli, MD², C Sluga¹, G Secco¹, S Gogorza¹, and M Martinez³. ¹ Department of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ²Chief of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ³Department of Surgical Pathology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: The objective of this study is to present four patients with the diagnosis of vulvar endometriosis, evaluated in the Service of Gynecology of the Italian Hospital of Buenos Aires.

Methods: Endometriosis is a common gynecological pathology characterized by growth of glands and endometrial stroma outside the endometrium. Implants are commonly found in the pelvis, but may appear in different sites. Vulvar endometriosis is a rare condition with an estimated incidence of less than 0.5%. It often develops after abdominal-pelvic surgery.

Results: Four women of reproductive age were diagnosed with vulvar endometriosis. The lesions were painful in all patients and surgery was performed in all cases. The mean follow-up was 5 years. No recurrences were observed.

Conclusions: Vulvar endometriosis is a relatively uncommon phenomenon, rarely localized to the vulva. Clinically, a painful bluish nodule can be observed in women of reproductive age. The diagnosis should be based

on review of previous medical records and clinical appearance; it should be confirmed by histological examination. Treatment is surgical resection with wide margins or laser therapy. A thorough gynecological evaluation should be performed, especially if the patient has symptomatic pelvic endometriosis.

Assessment of Efficacy of Er: YAG Laser Treatment for Female SUI Using 1 Hour Pad Test - Pilot Study with 12 Months Follow-Up

A Gaspar, MD^{1,2}, H Brandi, PhD, MD¹, S Maestri, MD^{1,3}, and D Luque¹. ¹Department of Laser Surgery Mendoza Hospital, Mendoza, Argentina. ²Medical Director Espacio Gaspar Clinic Mendoza, Argentina. ³Urogynecologist, Espacio Gaspar Clinic, Mendoza, Argentina.

Objectives: The scope of this study was to demonstrate the efficacy and safety of a non-surgical, minimally invasive Erbium laser (Er:YAG laser) treatment for stress urinary incontinence (SUI) and to compare the results to a control group.

Methods: Two groups were recruited: LASER GROUP with 43 patients. Aged 33-64 Average BMI: 27.4. They underwent thermal Er: YAG laser treatments. Patients received three treatment sessions with intervals of 1 month in between the sessions. CONTROL GROUP: with 29 patients aged 31-60. Average BMI: 26.7 received 2 weekly sessions of pelvic floor muscles exercises with perineometry, during three months. Only patients with valsalva leak point pressure (VLPP) > 60 mmHg were recruited. A standardized 1-hour pad-test was used to evaluate the efficacy of the treatment.

Results: Follow-ups were performed at 3, 6, and 12 months. The pad weight decreased in both groups at the 3-month follow-up. This was more pronounced in the laser group (66% - 72% - 70%) in contrast to the control group (58% - 47% - 29%). This effect remained constant up to the 12-month, while the results in the control group showed a diminishing trend.

Conclusions: Erbium laser for stress urinary incontinence is a safe and effective method for the management of SUI. Mid-term follow-up results show that the results can last for at least a year after treatment. Since the treatment is non-invasive, it could also be repeated once the results start diminishing.

Long-Term Experience with the Bidimensional Labia Minora Reduction

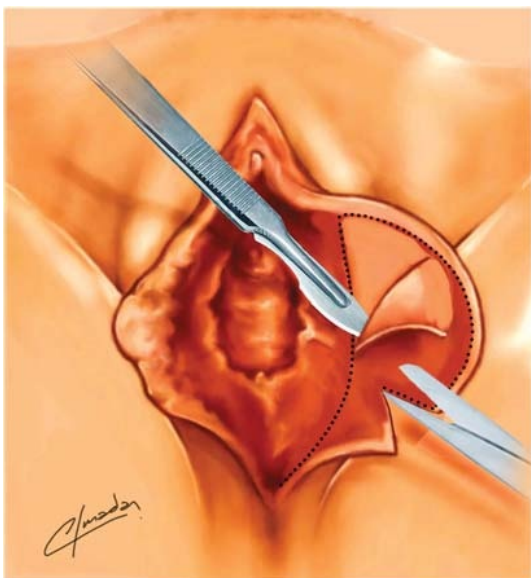
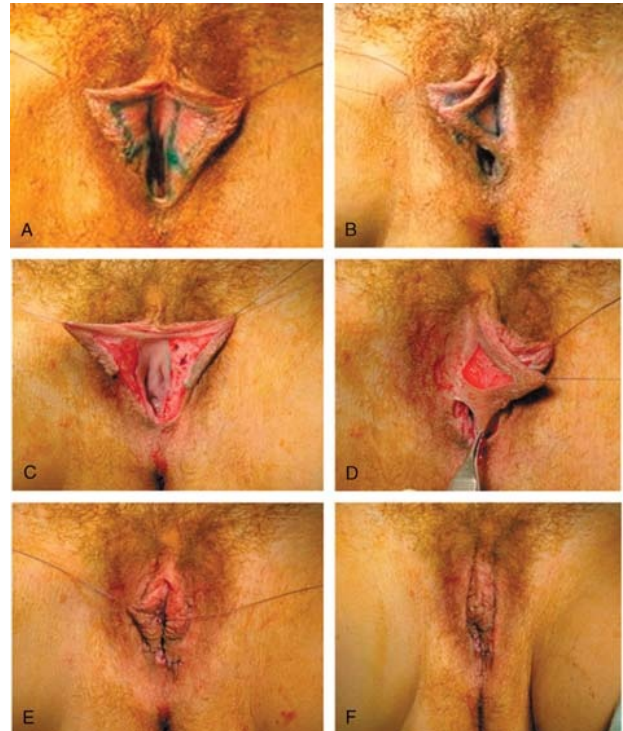
HF Mayer¹. ¹Plastic Surgery Department, Hospital Italiano de Buenos Aires, University of Buenos Aires School of Medicine, Buenos Aires, Argentina.

Objectives: To present clinical experience with the bidimensional technique.

Methods: A retrospective review of all patients' clinical records that underwent the bidimensional technique was undertaken. A long-term follow-up was carried out by telephone. Patients' overall satisfaction with the procedure and final result was rated on a scale of 1 to 5, where 1 was poor, 2 was fair, 3 was good, 4 was very good, and 5 was excellent.

Results: From October 2005 to December 2016, 36 women with an average age of 27 years (range 18-47) underwent this technique. In all patients, the wound healed very well. There were no reports of tip flap necrosis. Two patients had immediate postoperative bleeding and another one developed a small hematoma that drained spontaneously. One patient developed an infection that responded well to antibiotics. By a telephone survey, 22 patients rated the procedure and results as excellent, 10 patients as very good, and 2 as good. Two patients were not reached.

Conclusions: The bidimensional technique provides a tension-free closure and adequate vascularization to the healing edges of the superior labial flap, which reduces the chance of wound dehiscence. The associated resection of a full thickness posterior wedge avoids a festooned appearance and the resulting scar is posteriorly placed, providing excellent cosmetic results and long term overall satisfaction.



Vulvar Sudoriferous Gland Epithelial Tumors

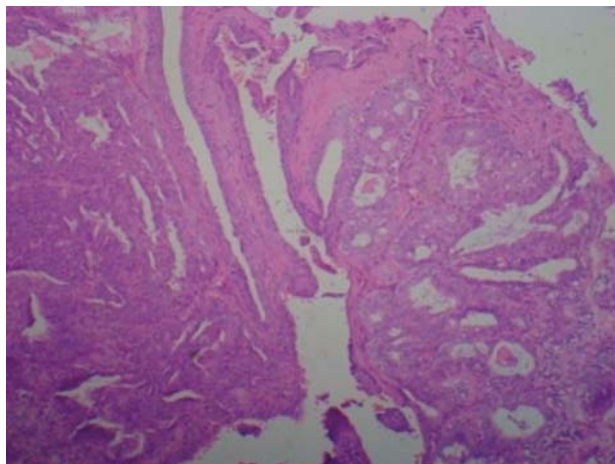
L Tinoco¹, S Carrillo², A Nicolalde³, D Tinoco⁴, V Tinoco⁵, R Tinoco⁶, D Ayala², R Masaquiza¹, and Z Paz¹. ¹Hospital Oncologico Solca-Quito, Quito, Ecuador. ²Ginecomast, Quito, Ecuador. ³Solca-Quito, Quito, Ecuador. ⁴Hospital San Francisco de Quito, Quito, Ecuador. ⁵Hospital Rodriguez Zambrano, Manta, Ecuador. ⁶Hospital Luz Elena Arismendi "Nueva Aurora", Quito, Ecuador.

Objectives: To identify the most frequent vulvar sudoriferous (sweat) gland epithelial tumors.

Methods: A descriptive epidemiological study was performed including women with vulvar sweat gland tumors surgically treated between 2004 and 2016 at Ginecomast and Oncologico Hospital "Solca" Quito.

Results: Ten apocrine gland tumors (hidradenoma papilliferum) were identified within the labia minora among women with an average age of 45 years (range 33 to 59). All were surgically excised. Eccrine gland tumors (syringomas and nodular hidradenoma) were identified among women with an age range of 28 to 68 years. Six syringomas were identified within the labia majora. The main symptomatology was pruritus. The treatment was surgical and in three patients an excisional biopsy and laser were performed. A scissile biopsy was performed on a nodular hidradenoma in a 28-year-old patient with a 2-cm. lesion. Histologically it was established as a clear cell variant.

Conclusions: Tumors of apocrine sweat glands were characterized by having associated ulceration, located mainly on labia minora. Eccrine glandular tumors were present on the labia majora and were characterized by intense pruritus. The treatment in extensive glandular lesions was surgical, with combined biopsy and laser performed in smaller lesions.



Hidradenitis Suppurativa

V Fonseca, MD¹. ¹Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

Objectives: Hidradenitis suppurativa is a chronic and recurrent inflammatory disease caused by occlusion and rupture of follicular units, in which the inflammatory response may secondarily involve the apocrine glands, leading to the formation of papules and nodules, which can progress to pustules, abscesses and fistulas. It is classified by Hurley's criteria stage I, II, III, according to the severity and extent of the disease. We present 3 women who required surgical treatment for severe hidradenitis suppurativa.

Methods: A retrospective review was performed, including three patients with severe hidradenitis suppurativa (Hurley's stage III) from the Vulvar Pathology Clinic of the Gynecology Service of HUCFF-UFRJ.

Results: Three patients 39, 41, and 60 years of age with Hurley's stage III hidradenitis suppurativa were included. Each had previously used antibiotics, zinc gluconate, isotretinoin and dapsone without satisfactory therapeutic response. Examinations revealed multiple interconnected sinus tracts, mons venus and perianal scarring, and abscesses involving the entire vulva and the bilateral inguinal area in each patient. All 3 were underwent surgical treatment consisting of wide excision or wide unroofing of affected areas - with healing by secondary intention or the use of skin grafts to close the defect.

Conclusions: Hidradenitis suppurativa is difficult to diagnose and manage. There is no ideal treatment that provides good functional and aesthetic results for all patients. In the cases presented, the surgical approach provided good results. Faced with the significant impact on the quality of life generated by this disease, it is up to the physician to use the best therapeutic strategies available.





Chronic Genital Malodor in the Absence of Infection: A Possible Manifestation of Olfactory Reference Syndrome

A Machefsky, MD^{1,2}, C Miller, MSW², KT Smith, PhD, CRNP,¹ P Nyirjesy, MD,¹ Drexel Vaginitis Center, Department of Obstetrics and Gynecology, Drexel University, Philadelphia, PA, USA. ²Department of Obstetrics, Gynecology and Women's Health, St. Louis University, St. Louis, MO, USA.

Objectives: While bacterial vaginosis (BV) is a common cause of vaginal malodor (VM), many affected women have no objective findings. These women present a challenge since there is no satisfactory diagnosis or treatment. Olfactory reference syndrome (ORS) is a psychiatric disorder characterized by a preoccupation with the belief that there is a foul offensive body odor, often from the

genital region. We studied women with chronic VM and no infection, as they may have ORS.

Methods: We performed a case-control study of 50 women with VM and 51 women with recurrent BV. All patients underwent a standardized evaluation. Historical and clinical variables were collected. Differences in demographic characteristics, medical/psychological comorbidities, and symptoms were assessed.

Results: The median age was 36.5 years in cases vs. 33.0 in controls. 40.0% vs. 29.4% were Caucasian. 16% vs. 10% were menopausal. The median duration of symptoms was 2 years vs. 1 year. All of the VM complained of malodor (described most commonly as fishy) compared to only 74.5% of the BV patients. 92% of the VM and 78.4% of the BV group had been previously treated for BV ($p = 0.06$). Both groups had similar rates of diagnosed psychiatric conditions (8% vs. 7.8%). After the initial evaluation showed no infection, 62% of the VM patients attempted some sort of intervention, with 79% reporting no change.

Conclusions: Women with VM are demographically similar to women with recurrent BV. Standard interventions to address abnormal odor are frequently unhelpful. These women may have a manifestation of ORS.

Recurrent Vulvovaginitis and its Relationship with Low-Grade Vaginal Intraepithelial Neoplasia in Ecuadorian Women

PA Yáñez, MD, PhD (c)^{1,2}, K Simbana, IR¹, L Gómez, IR¹, JA Duran, MD, PhD (c)^{1,2}, S Quintana, MD, PhD³, and E Terán, MD, PhD⁴. ¹Department of Clinical Pharmacology, Central University of Ecuador, Quito, Ecuador. ²Unit of Colposcopy and Pathology of the Lower Genital Tract, Provida Basic Hospital, Latacunga, Ecuador. ³Department of Gynecology and Obstetrics, Faculty of Medicine of Ribeirão Preto, University of Sao Paulo, Sao Paulo, Brazil. ⁴Colegio de Ciencias de la Salud, Universidad San Francisco de Quito, Pichincha, Ecuador.

Objectives: To investigate the association between recurrent vulvovaginitis with the presence of vaginal low-grade squamous intraepithelial lesions (LSILs) in Ecuadorian women.

Methods: This retrospective and descriptive study was performed in a group of 96 women attending the outpatient clinics at the Unit of Inferior Genital Tract Pathology and Colposcopy of Provida Basic Hospital in Latacunga, Ecuador between 2014 and 2016 for chronic itching of the vulva. Data from medical records were analyzed using the computer software Statistical Package for the Social Sciences (SPSS) 11.0.

Results: Out of 77 cases of histopathological samples, 92.2% ($n = 71$) presented with intraepithelial lesions. Vaginal LSIL was as follows: VAIN 1 64.8% ($n = 46$), squamous papillomas 28.2% ($n = 20$), condyloma 5.6% ($n = 4$). 7.8% of the patients had a negative result. In addition, on histology, the possible presence of human papillomavirus (HPV) was reported in 58.4% ($n = 45$).

Conclusions: This study shows that a large percentage of patients with recurrent vulvovaginitis also have benign histopathological alterations associated with HPV infection. A prospective study is necessary to explain the relationship between vaginal microbiota and HPV infection.

Diazepam Serum Levels are Minimal Following Vaginal Administration

L Edwards, MD¹. ¹Southeast Vulvar Clinic, Charlotte, NC, USA.

Objectives: To evaluate the systemic absorption of diazepam following vaginal use of diazepam for vulvodynia.

Methods: Fourteen consecutive women with vulvodynia treated with compounded 10 mg vaginal diazepam suppositories were assessed. One hour after insertion, serum diazepam levels were measured.

Results: Thirteen of the fourteen patients had undetectable levels of diazepam. One patient had nordiazepam level of .1 mg/mL, the lowest detectable level. No patient had side effects such as sedation that would be expected with systemic absorption of the diazepam.

Conclusions: Compounded 10 mg vaginal diazepam suppositories appear to produce minimal systemic absorption, so that driving following insertion is most likely safe, and addiction and withdrawal symptoms unlikely. Efficacy was not measured.

Histopathological Findings in Patients with Chronic Vulvar Itching: Experience in an Ecuadorian Population

JA Duran-Chávez, MD, PhD (c)^{1,2,3}, L Gómez, IR¹, K Simbana, IR¹, S Quintana, MD, PhD³, PA Yáñez, MD, PhD (c)^{1,2}, and E Terán, MD, PhD⁴.
¹Department of Clinical Pharmacology, Central University of Ecuador, Quito, Ecuador, ²Unit of Colposcopy and Pathology of the Lower Genital Tract, Provida Basic Hospital, Latacunga, Ecuador, ³Department of Gynecology and Obstetrics, Faculty of Medicine of Ribeirão Preto, University of Sao Paulo, Sao Paulo, Brazil, ⁴Colegio de Ciencias de la Salud, Universidad San Francisco de Quito, Ecuador.

Objectives: To investigate the association between chronic vulvar itching with the presence of vulvar low-grade squamous intraepithelial lesions (LSIL).

Methods: This retrospective and descriptive study was performed in a group of 33 women, attending to the outpatient clinics at the Unit of Inferior Genital Tract Pathology and Colposcopy of Provida Basic Hospital in Latacunga, Ecuador between 2014 and 2016 with chronic vulvar itching. A biopsy was performed in all 33 patients with pigmented lesions, and condyloma/verruccous lesions, to confirm the diagnosis. Data from medical records were analyzed using the computer software statistical package for the social sciences (SPSS) 11.0.

Results: The mean age was 28 ± 5 years (range 19 to 53). Out of 33 cases, 93.9% (n = 31) were confirmed to have LSIL on histology, with lichen simplex chronicus identified in the remaining 6.1% (n = 2). Additionally, the presence of human papillomavirus (HPV) was reported in 60.6% (n = 20).

Conclusions: This study suggests that the majority of women with vulvar LSIL complained of vulvar itching.

Pelvic Floor Dysfunction: Women's Sexual Activity at Risk

AE Sampietro¹ and ME Alcoba¹. ¹Austral University Hospital, Pilar, Buenos Aires, Argentina.

Objectives: Female sexual function is complex, involving physical, emotional, and psychological factors. Female patients with pelvic floor diseases may suffer from several sexual disorders and sexual life impairments. The aim of this study was to evaluate sexual dysfunction in female patients presenting with urinary incontinence (UI), pelvic organ prolapse (POP) or both.

Methods: A retrospective analysis was performed of a prospectively collected database of women referred to the pelvic floor section, who completed the Spanish validated pelvic organ prolapse/incontinence sexual questionnaire-12 (PISQ-12) at the first visit. Statistical analysis was performed to evaluate and compare sexual dysfunction between patients with UI, POP and both, as well as published data on the general population.

Results: 176 patients were identified, 98 (55%) who reported sexual activity were analyzed: 52 had UI (53%), 24 POP (25%) and 22 both (22%). Major sexual impairment (PISQ-12 < 30) was found in 42 patients (42.8%). The mean PISQ-12 (32.59 ± 7.2) score was 6 points lower than those reported in the general population from PISQ-validating studies (p < 0.05). When stratified by pelvic floor dysfunction, the UI group had higher PISQ scores, reflecting less sexual dysfunction than the POP and the UI + POP groups.

Conclusions: Sexual dysfunction is prevalent among patients suffering from UI and POP, and questionnaires are useful in recognizing these patients. The physical effect of prolapse and incontinence is one of the contributing factors for sexual dysfunction.

The Prevalence of High Tone Pelvic Floor Dysfunction with Symptomatic Vulvovaginal Atrophy

BK Lynn, MD¹, C Miller, MSW¹, J Thompson, RN¹, and EC Campian, MD¹.
¹Center for Sexual Health, Department of Obstetrics, Gynecology and Women's Health, Saint Louis University, St. Louis, MO, USA.

Objectives: Vulvovaginal atrophy (VVA) is a leading cause of dyspareunia in postmenopausal women. Clinical experience suggests that some women with VVA will also have high tone pelvic floor dysfunction (HTFPD). How often VVA and HTPFD coexist has not been studied. Treating VVA without treatment of HTPFD leaves a cohort of women still struggling with sexual pain. Our aim was to assess the frequency with which HTPFD coexists with VVA in women seen in a sexual medicine clinic as well as to determine if differences exist in women with VVA alone when compared to women with VVA/HTFPD.

Methods: A retrospective chart review was performed. Women seen for sexual disorders in a sexual medicine clinic were included. Previously collected

demographic data, pertinent past medical history, and Female Sexual Function Index (FSFI) scores were extracted and analyzed.

Results: Of 80 women with VVA, 31 (38.8%) were diagnosed with HTPFD. Co-existing conditions were similar between women with and without HTPFD. A greater proportion of women with HTPFD had a chief complaint of dyspareunia (93.5% vs. 69.4%; p = 0.02). A higher proportion of women with HTPFD had a history of endometriosis (16.7% vs. 2.1%; p = 0.05). No statistically significant differences emerged when comparing FSFI scores between women with and without HTPFD.

Conclusions: More than a third of women with VVA had HTPFD. Many clinicians don't routinely check for HTPFD. Clinicians may be under-treating HTPFD in women with VVA and limiting restoration of normal sexual function and painless intercourse.

Long-Term Outcome of Total Vestibulectomy

A David^{1,2}, B Diker, MD^{1,2}, D Zarfati, MD^{1,2}, and J Bornstein, MD, MPA^{1,2}.
¹Department of Obstetrics and Gynecology, Galilee Medical Center, Nahariya, Israel. ²Bar-Ilan University Faculty of Medicine, Nahariya, Israel.

Objectives: To evaluate long term follow-up of patients who underwent total (anterior and posterior) vestibulectomy over 10 years ago, by one surgeon.

Methods: The follow-up was conducted through face-to-face interviews with 32 patients who were operated before 2003 and chosen randomly. All of them were operated on by one surgeon (JB). The interviews tested the frequency of sexual intercourse, the degree of pain in carrying out various activities, satisfaction from the surgery's results, and willingness to recommend the surgery to other women.

Results: 100% of the patients experienced painful sexual intercourse at some point after surgery, and the median time was 4 months until first painless intercourse. Prior to surgery, introital penetration was the most painful activity to all patients, averaging 9.12 on a pain scale (0-10). It dropped to 0.47 currently (P < 0.001). Using a tampon, post-coital urination, and other activities were also improved significantly after surgery. None of the patients reported reappearance of pain over time. 94% of the operated patients were highly satisfied of the operation they underwent, 97% would undergo the surgery again knowing the outcome, and 100% would recommend it to a friend suffering from the same condition.

Conclusions: Our work demonstrated high surgical success rates of total vestibulectomy. We did not find any evidence of deterioration or resurgence of pain over more than a decade after the surgery, and even witnessed an improvement. Overall patient satisfaction was high, and the general attitude toward the surgery was positive.

Improvements in FSFI Scores using Vaginal CO2 Microablative Laser

M Sophocles¹. ¹University Hospital of Princeton, Princeton, NJ, USA.

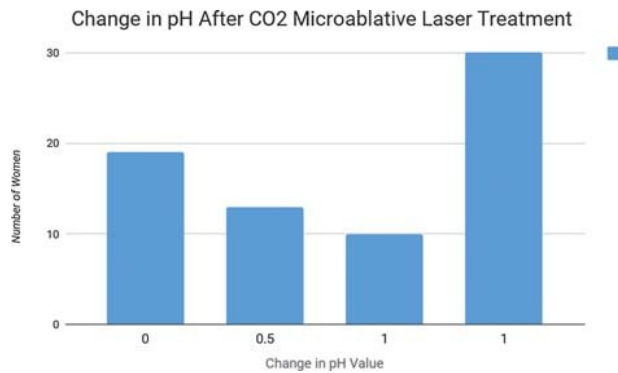
Objectives: To examine the clinical efficacy of a carbon dioxide (CO2) laser treatment in improving female sexual function, using a validated Female Sexual Function Index (FSFI) questionnaire.

Methods: 62 postmenopausal women aged 46-75 underwent three SmartXide (DEKA, Florence, Italy) vaginal treatments six weeks apart. Patients completed FSFI questionnaires before and after the treatment cycle. Half the women received laser treatments alone (Group 1) and half received concurrent therapy with either vaginal estrogen or ospemifene (Group 2).

Table 1. FSFI prior and post MLT treatment study results and individual domain results

	FSFI Scores*	Desire Scores*	Arousal Scores*	Lubrication Scores*	Orgasm Scores*	Satisfaction Scores*	Pain Scores*
Raw Percentages of Improvement	(51/62) 82.3% showed an increased FSFI score.	(34/62) 54.8% showed increased sexual desire.	(39/62) 62.9% showed increased sexual arousal.	(46/62) 74.2% showed increased lubrication.	(32/62) 51.6% showed enhanced orgasms.	(38/62) 61.3% showed increased sexual satisfaction.	(43/62) 69.4% showed less pain with vaginal penetration.
Mean of Difference between Pre and Post Scores with 99% Confidence	6.49 ± 2.79	0.72 ± 0.36	0.73 ± 0.57	1.58 ± 0.64	2.8 ± 0.58	0.74 ± 0.52	1.78 ± 0.68
Number of Participants (n)	62	62	62	62	62	62	62
t-statistic and degrees of freedom (df)	6.19 with 61 df	5.27 with 61 df	3.37 with 61 df	6.57 with 61 df	12.87 with 61 df	3.78 with 61 df	6.95 with 61 df
p-value	< 0.001	< 0.001	< 0.002	< 0.001	< 0.001	< 0.001	< 0.001
Statistical Significance	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01	Yes, at α = 0.01

FSFI SCORES PRE- AND POST-CO2 LASER TREATMENT.
 *Each section compared pre- and post-treatment scores using a Matched Pairs T-test.



Results: As a primary analysis, we compared pre- and post-laser FSFI scores for each of the six subdomains and the overall score for statistical significance using a matched pairs t-test. Each of the seven p-values demonstrated statistical significance with $p < 0.01$. As a secondary analysis, we tested the difference in the FSFI scores between Groups 1 and 2. The mean difference was calculated using a 95% confidence interval and was found to be 2.09 ± 4.23 . A two-sample t-test resulted in a t-statistic of 1.009 with degrees of freedom of 30. A p-value greater than 0.20 but less than 0.15 was obtained.

Conclusions: 82.3% of patients showed statistically significant improvement in overall FSFI. All subdomains showed statistically significant change as well. In our secondary analysis, we had presumed an additive or synergistic effect from dual therapy but statistical analysis did not support our hypothesis. Vaginal CO2 laser therapy is a promising clinical tool; higher powered sham and head-to-head comparison studies are needed.

Connecting the Dots: Relationships Between Review of Systems Responses and Chronic Urogynecologic Pain

A Hesson, MD, PhD¹, AG Sammarco, MD¹, M Berger, MD, PhD¹, and HK Haefner, MD¹. ¹Department of Obstetrics and Gynecology, Michigan Medicine, Ann Arbor, MI, USA.

Objectives: Patients with functional disorders have characteristic responses to the review of systems (ROS) that can be used to facilitate diagnostic assessment and treatment allocation. We aimed to identify patterns of ROS symptoms affirmed/denied by genitourinary pain patients and assess potential associations with chronic pain severity and narcotic use.

Methods: New patients referred to a urogenital/pelvic pain clinic (N = 158) completed standardized questionnaires, including ROS. ROS symptoms reported by ≥ 10 patients were subjected to multiple correspondence analysis (MCA). Patient reports of symptoms in two contrastive clusters identified in the MCA were summed, creating two scores which were then individually correlated with patient visual analogue pain scale (VAS, 1–10) responses and compared across self-identified narcotic users/non-users.

Results: Two MCA dimensions of variance collectively accounted for 21.4% of the ROS response variation. The first dimension contrasted symptom affirmations and denials, while the second identified two symptom affirmation clusters: 1) uro-psych (N = 20 symptoms, e.g., dysuria, frequency, urgency, anxiety, premenstrual syndrome) and 2) thoraco-abdominal (N = 32 symptoms, e.g., nausea, diarrhea, chest pain, and cough). There was a significant positive correlation between VAS and thoraco-abdominal scores ($R = 0.20, p = 0.02$), but not uro-psych scores ($R = 0.15, p = 0.10$). Total number of symptom affirmations also correlated positively with VAS responses ($R = 0.21, p = 0.02$). Narcotic users had more uro-psych, thoraco-abdominal, and overall symptom affirmations (x-users = 14.6, x-non = 9.15; $p < 0.01$) compared to non-users.

Conclusions: Greater numbers of reported symptoms on ROS—particularly those related to thoraco-abdominal concerns—are associated with more severe chronic pain in urogenital/pelvic pain patients. Narcotic users had significantly more cross-category ROS symptom affirmations than non-users.

Refining a Pain Mapping Tool for Vulvodynia

S Johns¹, M Jantos², and E Baszak-Radońska³. ¹BNurs, MMid, School of Nursing and Midwifery, University of South Australia, Adelaide, S Australia.

²Behavioural Medicine Institute of Australia & Department of Human Anatomy, Medical University of Lublin, Poland ³Terpa Clinic, Lublin, Poland.

Objectives: The study sought to establish the validity of pain mapping points that would reliably differentiate between women with vulvodynia, bladder pain syndrome (BPS), general gynecology, and asymptomatic controls.

Methods: A total of 320 pain maps were included in the study. Of these 238 were of women diagnosed with vulvodynia. Of these 238 vulvodynia cases, 119 were diagnosed with vulvodynia only and 119 with vulvodynia and BPS. These groups were compared with 29 women diagnosed with BPS only, 21 general gynecology cases, and 32 asymptomatic controls. A total of 52 points were assessed in three anatomical regions (Map A, B & C). The study was approved by the University of South Australia's Human Research Ethics Committee.

Results: All groups were comparable in terms of age and parity. The summary of pain scores for all groups are shown in Figure A. Pain mapping score comparisons of Vulvodynia, BPS, Vulvodynia and BPS, General Gynecology & Controls. On Map A women with vulvodynia only reported higher scores than those with vulvodynia and BPS or BPS only. On Map B and C vulvodynia and BPS reported higher scores. Thirteen points on Map A and all points on Map B and Map C differentiated between pain groups and controls. For all pain groups the highest pain ratings were reported in the paraurethral area.

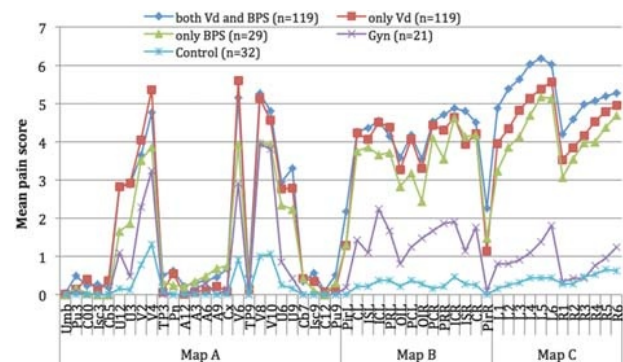


FIGURE. Comparison of mean pain scores for Vd, BPS and controls

Conclusions: For diagnostic and classification purposes the focus to date has been on the external urogenital area. Insufficient attention has been directed to other sources of symptoms and pain, such as the pelvic muscles and the paraurethral area that reliably and consistently differentiate between asymptomatic and symptomatic women.

Keratin Pearls as a Cause of Clitorodynia: A Series of Five Cases

A Goldstein¹, L Mitchell¹, A Gumer², and G Yazdy³. ¹The Center for Vulvovaginal Disorders, Washington, DC, USA. ²Columbia University Department of Obstetrics and Gynecology, New York, NY, USA. ³The George Washington University Department of Obstetrics and Gynecology, Washington, DC, USA.

Objectives: Clitorodynia is a form of localized vulvodynia. Limited research has been published regarding the etiologies clitorodynia, however, several conditions have been associated with clitorodynia including lichen sclerosis, vestibulodynia, multiple sclerosis, and pudendal neuralgia. A keratin pearl is a focus of central keratinization within concentric layers of squamous cells. It is thought to be a result of accumulation of smegma, which is the combination of secretion from sebaceous glands and desquamated epithelial cells beneath the prepuce in females or the foreskin in males. We describe the cases of five women who presented with clitorodynia and associated keratin pearls.

Methods: Retrospective review including five women who presented to a vulvar disorders clinic with clitorodynia with associated keratin pearls.

Results: Our patients presented with three months to fourteen years of clitoral pain. All complained of both non-provoked and provoked clitoral pain exacerbated by touch and certain movements. One patient also had sensations consistent with persistent genital arousal disorder (PGAD). All patients had adhesions between the prepuce and glans clitoris and keratin pearls. (Figure 1). Mild erythema and inflammation were present (balanitis) and there was clitoral allodynia. Following application of a topical anesthetic, a lacrimal probe was used to lyse the adhesions and excise the keratin pearls. All five patients reported improvement in their clitorodynia; three having complete remission.

Conclusions: Clitorodinia is a poorly understood and under-reported form of vulvar pain. Our five cases demonstrate that adhesion and keratin pearls may be a cause of clitorodinia. In addition, adhesiolysis and removal of keratin pearls can provide improvement in clitoral pain.

Lessons from Postmenopausal Patients about Estrogen and Excisable Vulvar Pain – A Case Series

MF Goetsch, MD, MPH¹. ¹Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland, OR, USA.

Objectives: To describe cases of localized vulvodynia that demonstrate estrogen sensitivity, and the utility of aqueous lidocaine for diagnosis, and the benefits of excision for pain relief.

Methods: Five patients, seen between 2013 and 2016 with severe dyspareunia or severe chronic unprovoked vulvar pain, are presented. Criteria: several minutes of 4% lidocaine topical solution extinguished severe vestibule allodynia and pain, and surgical excision corrected this pain 80-100%.

Results: Three patients had provoked pain after 1-2 years without estrogen; two had severe unprovoked pain after 30 & 17 years without estrogen. Patient #1 had had postpartum vestibular dyspareunia at age 32, cured with a localized superficial vestibulectomy, but after menopause vestibulodynia recurred during two periods without estrogen, and resolved with systemic estrogen therapy. Patients #2 and 3 were breast cancer survivors who had localized vestibulodynia amenable to office excisions of peri-Bartholin duct mucosa, correcting their severe dyspareunia. Patients #4 and 5 had late-age debilitating vulvar pain that responded partially to estrogen, and excision corrected the pain in one and reduced it 80% in the other.

Conclusions: The vulvar vestibule is sensitive to dramatic drops or prolonged absence of estrogen. Postpartum anovulation can initiate localized provoked vulvodynia, which, once corrected, can return with estrogen depletion of menopause. Prolonged estrogen lack after menopause can first cause severe dyspareunia but then progress to severe unprovoked pain. Late postmenopausal estrogen supplementation can ameliorate pain, but surgical excision may be an option in severe cases or in breast cancer survivors for whom estrogen is contraindicated.

Sexual Satisfaction in Women Under 45 Years with Vulvar Dermatoses that Obtain Colposcopy Service at the Ambulatory Attention Center and Day Hospital “El Batán” During the Period January-June 2016

V Argote¹. ¹Ministerio de Salud Pública del Ecuador, Quito, Ecuador.

Objectives: To determine the sexual satisfaction and alterations of the sexual function in women under 45 years old who came for vulvar dermatoses, using the Female Sexual Function Index (FSFI).

Methods: A cross-sectional descriptive observational study was performed in 50 women who attended the Service of Pathology of the Lower Genital Tract and Colposcopy of the Center of Ambulatory Attention and Day Hospital “El Batán”, between January and June of 2016 who agreed to participate in the investigation.

Results: The mean age of patients was 42 years. The majority lived in an urban area (83.75%). 96.58% were married. 49.57% were multiparous. 57.26% had a secondary education. A sexual satisfaction disorder was present in 46% (n = 23), within which a severe lubrication disorder was observed in 47.83% (n = 11), a moderate disorder in the sexual desire 69.56% (n = 16), excitation in 52.17% (n = 12), and orgasm in 43.48% (n = 10). There was a statistically significant relationship between the level of sexual satisfaction and the presence of vulvar condylomata (p = 0.019).

Conclusions: The sexual satisfaction of patients presenting with vulvar dermatoses was altered in 46% of cases, mainly due to an alteration in sexual arousal.

The Burden and Impact of Moderate-to-Severe Genital Psoriasis on Female Patients

J Cather, MD¹, A Potts-Bleakman, PhD², C Ryan, MD³, J Ling Poon, PhD⁴, B Malatestinic, PharmD, MBA², A Naegeli, DrPH, MPH², and S Fretzin, MD⁵. ¹Modern Dermatology, Aesthetics Center, Dallas, TX, USA. ²Eli Lilly and Company, Indianapolis, IN, USA. ³St. Vincent's University Hospital, Dublin, Ireland. ⁴Evidera, Bethesda, MD, USA. ⁵Indiana University School of Medicine, Indianapolis, IN, USA.

Objectives: Genital psoriasis (GP) is common, impacting patients' sexual and physical activity, as well as health-related quality of life (HRQoL). We conducted a survey to better understand symptoms and burden of GP in female patients.

Methods: We conducted semi-structured phone interviews with 20 US patients, aged ≥ 18 years, with a physician diagnosis of plaque psoriasis (duration ≥ 6 months) and self-reported, dermatologist confirmed current/recent (≤ 3 months) moderate-to-severe GP (per Patient Global Assessment ≥ 4). We designed interviews to identify the impact of GP symptoms on sexual health and HRQoL. We coded and analyzed transcripts to identify key themes and responses. Here we report results for the 11 female patients, who were on average 49.5 years of age with 5.1 years of GP.

Results: Common GP symptoms were itch (100%), discomfort (100%), redness (91%), stinging/burning (91%), pain (73%), and scaling (73%). Itch (55%), pain (36%), and stinging/burning (36%) were most bothersome. Common nonsexual impacts of GP on HRQoL were mood/emotion (91%), physical activities (64%), daily activities (64%), and general impacts not covered by other categories (64%). Patients most frequently reported the following sexual impacts of GP: worsening GP symptoms after sexual activity (73%), physical effects on sexual experience (73%), decreased sexual frequency (73%), avoidance of sexual relationships (64%), and reduced sexual desire (45%).

Conclusions: In these qualitative interviews, the most burdensome symptoms of GP in female patients were itch, pain, and stinging/burning. In the majority of women we interviewed, GP negatively impacted HRQoL, including sexual and nonsexual impacts, and requires assessment and follow-up.

Assessing Patient Satisfaction and Compliance with Compounded Clobetasol Propionate 0.05% and Estradiol 0.01% for the Management of Lichen Sclerosus with Coexisting Genitourinary Syndrome of Menopause

ML Racher, MD^{1,2}, LS Newton, MD², T Ivey, APRN^{1,2}, and CH Gauss, MS³. ¹Center for Vulvar Disorders, University of Arkansas for Medical Sciences, Little Rock, AR, USA. ²Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR, USA. ³Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR, USA.

Objectives: The aim of this study was to assess both patient satisfaction and compliance with compounded clobetasol propionate 0.05% and estradiol 0.01% in an emollient base for treatment of lichen sclerosus (LS) with coexisting genitourinary syndrome of menopause (GSM) compared to prior treatment regimens of separate commercially available preparations of clobetasol ointment and estrogen cream.

Methods: Seventeen women from the Center for Vulvar Disorders at the University of Arkansas for Medical Sciences were identified for study participation. Patients were given a prescription for compounded clobetasol propionate 0.05% and estradiol 0.01% in an emollient base. After a treatment trial with the compounded medication, 14 of the 17 subjects completed a short survey about their level of satisfaction and compliance. Descriptive statistics were obtained, and the Wilcoxon signed rank test was used to compare the compliance level for the compounded medical regimen and the previous medical regimen.

Results: Most patients were very satisfied overall with the compounded medication regimen (85.7%) and were more satisfied with the compounded medication compared to their previous medication regimen (92.9%). The compliance levels of the two medication regimens were statistically significantly different (p = 0.0010) with compliance for the compounded medication regimen being higher.

Conclusions: As satisfaction and medication compliance levels appear to be higher for the compounded clobetasol 0.05% and estradiol 0.01% than for separate preparations of commercially available clobetasol ointment and estrogen cream, the compounding of these medications for treatment of LS with coexisting GSM may warrant further investigation.

The Link Between Management, Compliance, and Clinical Outcomes in Women with Vulvar Lichen Sclerosus

T McClatchey¹, J Kohn¹, and A Vyas, MD². ¹Baylor College of Medicine, Houston, TX, USA. ²Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX, USA.

Objectives: To investigate the relationship between strength of topical steroid regimen, treatment compliance, and clinical outcomes in women with vulvar lichen sclerosus (VLS).

Methods: Retrospective case series of women with VLS at a vulvovaginal specialty clinic from 2012-2017. IRB approval was obtained. Data were extracted by chart review. Analysis included descriptive statistics and panel data logistic regression.

Results: 151 women attended 788 visits (median 5 per patient, range 1-17). At presentation, the mean age was 61 ± 11 years (range 31-90), and 22% were premenopausal. 77% were Caucasian, 4% Hispanic, 2% African-American, 1% Asian, and 16% unidentified. 52% had atopic disease, 34% had hypothyroidism, and 24% were nulliparous. There was no significant difference in likelihood of clinical improvement between super-high and high potency steroid ($p = 0.67$). Clinical improvement was more likely with use of super-high or high-potency steroid compared to medium- or low-potency steroid (OR 3.8, $p = 0.03$). Patients reported perfect compliance with topical steroid at 65% of visits. 27% reported imperfect use, and 8% reported no use at all. Compared to no use, perfect use strongly predicted clinical improvement (OR 9.8, $p < 0.01$); less-than-perfect use also predicted clinical improvement but to a lesser extent (OR 4.9, $p = 0.04$). At presentation, 48% were not sexually active due to pain. Of these, 53% became sexually active during follow-up.

Conclusions: Women with VLS are ten times more likely to improve clinically with perfect use of topical steroid, but only four times more likely to improve with imperfect use. Super-high and high-potency steroids demonstrate equivalent outcomes.

Plasma Cell Vulvitis (Zoon's Vulvitis) in 3 Patients

A Ramirez¹, C Sluga², C Marchitelli, MD³, M Martinez⁴, M Peremateu⁵, A Wernicke⁶, and S Gogorza⁷. ¹Hospital Angeles del Pedregal, Mexico City, Mexico. ²Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ³Chief of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁴Department of Surgical Pathology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁵Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁶Pathology service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁷Chief of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: To present 3 cases of plasma cell vulvitis (PCV) evaluated at the Gynecology Service at the Italian Hospital in Buenos Aires.

Methods: Three patients were seen complaining of dyspareunia (vaginal stinging pain). During their physical examination, the vaginas appeared erythematous, shiny, with well-defined vestibular plaques. A biopsy was consistent with plasma cell vulvitis (Zoon's vulvitis). The patients were managed with clobetasol and estrogen vaginal cream.

Results: With this treatment, the patients (ages 32, 56, and 57 years) all had partial remission of their symptomatology. They experienced exacerbations during their follow up. Nevertheless, all the patients experienced some degree of improvement.

Conclusions: Plasma cell vulvitis (PCV) or Zoon's vulvitis is a benign disease without a known cause. Multiple factors have been found to predispose patients to this condition, such as chronic infections, trauma, heat, profuse sweating, and lack of hygiene (accompanying an inflammatory response). This disease affects women between 50 and 80 years of age. The clinical signs are bright erythematous well defined, unique, or multiple plaques in the vestibular mucosa, labia minora, and periurethral areas. The accompanying symptoms are pruritus, pain, stinging, and dyspareunia. Nevertheless, sometimes it can be asymptomatic. The diagnosis of this disease is performed by observing the distinctive histopathology of a dense lichenoid infiltrate, which is mainly constituted by plasma cells, a vascular proliferation, dilation of capillary vessels, extravasation of erythrocytes, and hemosiderin deposits. While a variety of treatments have been tried for plasma cell vulvitis, many patients do not respond to them.

Review of Women Diagnosed with Plasma Cell Vulvitis Treated by the Harvard Vanguard Vulvovaginal Service

B Goldbaum¹. ¹Harvard Vanguard Medical Associates Vulvovaginal Service, Boston, MA, USA.

Objectives: To review the medical records of all women with plasma cell (Zoon's) vulvitis treated by the Harvard Vanguard Medical Associates Vulvovaginal Service from 2002 through 2016 with respect to presenting symptoms, treatment modalities, comorbidities, and long term follow-up.

Methods: Record review of all women with a diagnosis code for plasma cell vulvitis resulted in 32 who met inclusion criteria, which included: biopsy proven disease, referral to our specialty service, and age over 18. Age at diagnosis,

presenting symptoms, number of visits and therapeutic treatments were analyzed. Women were followed longitudinally with evaluation of disease response to various treatments.

Results: The mean age at diagnosis was 56.5 (range 28-85). Women presented with multiple symptoms. Most common were: dyspareunia (22), burning (16), pruritus (13), contact dysuria (10), vaginal discharge (9), pain (9), irritation (5) and bleeding (3). The average number of visits was 11.5 (range 2-51). Treatment modalities included: topical, intravesicular, vaginal, intramuscular and oral steroids; compounded clobetasol/oxytetracycline/nystatin cream (Zoon's paste); topical calcineurin inhibitors; topical and systemic estrogen; pelvic floor physical therapy; acupuncture; fluconazole and clotrimazole for suppression of candida; gabapentin and amitriptyline for neuropathic pain. The most commonly used and effective treatment was clobetasol ointment. The average number of months in treatment was 43 with 18 women in ongoing care.

Conclusions: Plasma cell vulvitis is difficult to treat and is commonly associated with sexual dysfunction as well as vulvar and vaginal symptoms. Multiple treatment approaches are necessary. Although women usually improve, most require long-term treatment and monitoring.

Evaluating the Benefit of Quadrivalent HPV Vaccine on Genital Warts in Opportunistic Vaccination Setup

S Lurie, MD^{1,2}, Y Mizrahi, MD^{1,2}, G Chodlick, MD^{2,3}, R Katz^{2,3}, and E Schejter, MD⁴. ¹Department of Obstetrics & Gynecology, Edith Wolfson Medical Center, Holon, Israel. ²Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. ³Medical Informatics Department, Maccabi Health Services, Tel Aviv, Israel. ⁴Cervical Clinic, Maccabi Health Services, Tel Aviv, Israel.

Objectives: Genital warts are the most common sexually transmitted disease and have a detrimental impact on quality of life. Genital warts could be prevented by prophylactic human papilloma virus (HPV) vaccination. To study the real-life benefit of opportunistic HPV vaccination setup on age and gender specific incidence of genital warts.

Methods: A register-based population cohort study was performed from the second largest publicly funded health-care provider in Israel, during two time frame intervals: 2006-2008 (pre-vaccination effect period) and 2013-2016 (post-vaccination effect period), with an average annual number of members of 1,765,481 and 2,042,678 in the years 2006-2008 and 2013-2016, respectively. Main outcomes and measures: genital warts incidence.

Results: Among females, the annual incidence of genital warts per 100,000 women decreased from 210.43 to 146.8 (OR 0.69, 95%CI 0.66-0.72, $p < 0.001$) between pre- and post-vaccination effect period with absolute risk reduction of 63.62 cases per 100,000 women per year. Among males, the annual incidence of genital warts per 100,000 men decreased from 262.85 to 234.01 (OR 0.88, 95%CI 0.86-0.91, $p < 0.001$) between pre- and post-vaccination effect period with absolute risk reduction of 28.84 cases per 100,000 men per year.

Conclusions: We have shown that there is a potential benefit in reducing the incidence of genital warts even in an opportunistic setup. This information might be relevant for health-care providers in countries where national immunization programs do not include HPV vaccines.

Radiofrequency Treatment in Patients Under 21 Years Old with Florid Vulvar Condyloma Resistant to Conservative Treatments

C Seira¹, M Piccone¹, B Perazzo¹, and G Castro¹. ¹Medica, Buenos Aires, Argentina.

Objectives: Human papillomavirus (HPV) infection is the most prevalent sexually transmitted disease worldwide. Clinical treatment of anogenital warts is conservative, however, in extreme cases conservative therapy is insufficient and surgical excision is required. The objective of this study is to present four patients under 21 years of age with florid vulvar condyloma, who were treated with radiofrequency excision after topical treatments with imiquimod 5% cream or topical trichloroacetic (TCA) acid failed.

Methods: Retrospective review including 4 patients with florid vulvar condyloma.

Results: All patients attended the public hospital, were under 21 years old, non-immunized with HPV vaccine, non-smokers, without co-morbid diseases, with sexual initiation at age 15 and 2 sexual partners. The outstanding feature in each case included exacerbation with increasing expression of the condyloma despite treatment. Four patients of 16, 17, 18 and 20 years respectively received local destructive treatment with 80% TCA acid for 2 to 3 months. Subsequently, all of them received imiquimod 5% 3 times per week, for 6 months. In view of the lack of response to conservative treatments, all patients were referred to our public

hospital in Buenos Aires and a shaving procedure was performed with Radiofrequency. This is the only device available in our public hospital for the treatment of condyloma. Patients are free of disease after 12 months of follow-up.

Conclusions: Radiofrequency represents a good alternative treatment for vulvar condyloma in young patients in cases of non-response to more conservative treatments.

Vulvar Telangiectasia: An Important Warning Sign of Excessive Topical Steroid Use

EE Eppsteiner, MD¹. ¹Department of Women's Health, Cooley Dickinson Healthcare, Northampton, MA, USA.

Objectives: To analyze three cases of vulvar telangiectasia in association with topical steroid use.

Methods: This study reviews three cases of vulvar telangiectasia related to superpotent topical steroid use. The women in this study presented to a community hospital vulvar disease clinic for routine management of vulvar dermatoses. All three women were using superpotent topical steroids at the time of their initial visit. Following an initial diagnosis of vulvar telangiectasia, each woman was tapered to the use of a lower potency steroid and was followed no less often than every three months with visual inspection and review of symptoms.

Results: All three women showed improvement or resolution of telangiectasia within three months of switching to a lower potency topical steroid, while maintaining symptomatic and architectural control of their underlying vulvar dermatoses.

Conclusions: Classically, the first line therapy for vulvar lichenoid dermatoses involves the use of superpotent topical steroids. Topical steroids can have deleterious effects on the vulvar skin when used too frequently or in formulations with excessive potency over extended periods of time. Vulvar telangiectasia is one particular effect. This study emphasizes the need for regular follow up for patients undergoing treatment with superpotent topical steroids, as well as the importance of provider recognition of steroid effects and adjustment of therapy to avoid continued insult to the vulvar skin.

The Prevalence of Clitoral Adhesions in Women Presenting to a Sexual Medicine Practice

L Aerts, MD, PhD¹, R Rubin, MD², A Winter, MD², S Goldstein, BA, IF², and I Golstein, MD, IF². ¹Department of Obstetrics and Gynecology, University Hospitals Geneva, Geneva, Switzerland. ²San Diego Sexual Medicine, Alvarado Hospital, San Diego, CA, USA.

Objectives: Physical examination of the clitoris during gynecological examination involves concomitant cephalad preputial retraction to evaluate the presence of the clitoral glans corona. Failure to see the corona implies that there are adhesions of adjacent prepuce skin to the glans covering the corona. The presence of clitoral adhesions is especially relevant in women with clitorodysplasia, sexual pain concerns and persistent genital arousal disorder. Beneath the clitoral adhesions, an underlying balanitis may exist that is perpetuated by a closed-compartment environment, often with several millimeter-sized keratin pearls observed lying underneath the adhesions. Since physical examination of the glans clitoris is not routinely performed by health care providers during the clinical examination, there are limited data on the prevalence of clitoral adhesions.

Methods: Vulvoscopy photographs taken in our sexual medicine practice from 2007–2015 were reviewed and evaluated for the presence of clitoral adhesions by two independent reviewers. Criteria for clitoral adhesions included: clitoral glans fully visualized, photograph in good focus, and cephalad preputial retraction noted.

Results: 1261 vulvoscopy photographs were reviewed and 767 photographs were considered adequate. Clitoral adhesions were suspected in 175 women (23%).

Conclusions: More than one in five women attending a sexual medicine practice has clitoral adhesions. We strongly encourage health care providers to carefully examine the clitoris with magnified view and ensure visualization of the corona by retracting the clitoral prepuce as a routine part of the gynecological examination. Understanding normal clitoral anatomy is a key part to being able to identify and diagnose clitoral disorders when they arise.

Diagnosis of Genital Infection with PCR Technique and the Relationship to Premature Birth in Patients Admitted to Santiago Oriente Hospital Between January 2015 and January 2016

M Acevedo¹, and A Díaz². ¹Obstetrics and Gynecology Postgraduate Program, University of Chile, Santiago, Chile. ²Department of Obstetrics and Gynecology, Santiago Oriente Hospital, Santiago, Chile.

Objectives: To describe the epidemiological profile of pregnant women with genital tract infections detected by polymerase chain reaction (PCR) technique, results of the examination, treatments received and the association between the presence of infectious agents and preterm birth.

Methods: The identification of the total PCR Pack Pregnant performed between January 2015 and January 2016 were obtained from the records of the Laboratory of the Santiago Oriente Hospital. The patients' clinical records were then requested and their epidemiological profile, treatments received, and obstetric results were reviewed. The data were tabulated and analyzed using the Excel 2010 program.

Results: 197 PCR results were analyzed, with 143 positive results. Patients with preterm birth had more PCR + testing, especially with Ureaplasma urealyticum, as well as a higher amount of chorioamnionitis associated with PCR + for Ureaplasma parvum. The number of patients treated with antibiotics according to the isolated agent was low in both groups.

Conclusions: The findings are very similar to those described in the literature, both the isolated germs and the low antibiotic coverage given to patients with positive tests, which makes us consider the need to generate strategies to follow up our patients to ensure they receive the appropriate managements for their clinical conditions.

Human Papillomavirus-Induced Squamous Intraepithelial Lesions in Vulvar Lichen Planus

O Reich¹. ¹Dept. Obstet/Gyn, Medical University of Graz, Austria Eberz B. General Gynecology Practice, Mürrzuschlag, Austria Regauer S. Institut of Pathology, Medical University Graz, Graz, Austria.

Objectives: Approximately 50% of vulvar cancers arise after transforming infections with human papilloma virus (HPV) in precursor squamous intraepithelial lesions (SILs). Lichen planus (LP)-associated vulvar cancers are typically HPV negative and arise in differentiated vulvar intraepithelial neoplasia (d-VIN).

Methods: An index case of vulvar high-grade squamous intraepithelial lesions (HSIL) in a patient with LP prompted this 12-year retrospective analysis to study the frequency of HPV-induced SILs. 785 biopsies of 584 patients with vulvar LP were analyzed. All squamous intraepithelial lesions were analyzed for p53 and p16 overexpression and for the presence of 32 HPV DNA subtypes.

Results: Nine (1.6%) of 584 women had lichen planus (papular (3) and mucosal erosive LP (6)). High-grade squamous intraepithelial lesions (HSILs) were present in 7 patients and low-grade squamous intraepithelial lesions (LSILs) were present in 2 patients. All SIL harbored HPV16-DNA and showed p16-overexpression. Concomitant immune suppression included T-suppressor lymphocyte deficit (1), and cortisone therapy (systemic (1), and topical (2)). HSILs regressed spontaneously in 1/7 or after imiquimod therapy (3/7). The remaining 3/7 women with erosive LP discontinued imiquimod because of side effects and had laser destruction (1), skinning vulvectomy (1), and surgery (1) for definitive treatment. Two women had recurrent vulvar SILs, and 1 woman progressed to invasive squamous cell carcinoma (SCC). In the same patient population, 16 of 584 women had d-VIN, with 9 of 16 progressing to SCC.

Conclusions: HSILs in patients with vulvar LP are rare and may occur in the setting of various risk factors. If clinical suspicion arises, biopsy and histological examination assist in correct etiologic classification of a precancerous lesion and subsequent therapy decisions. The minimal risk for HSIL development in vulvar LP patients should not preclude therapy of LP.

hELP! A Multi-Center Four Armed Pilot Randomized Controlled Trial for Vulvar Erosive Lichen Planus: Results and Lessons Learned

R Simpson¹, R Murphy², and K Thomas¹. ¹Centre of Evidence Based Dermatology, University of Nottingham, UK, ²Sheffield Teaching Hospitals NHS Trust, Sheffield, UK.

Objectives: Erosive lichen planus affecting the vulva (ELPV) is distressing and impacts upon quality of life. First-line therapy is often inadequate and evidence for second-line treatments is poor. 'hELP' (systemic therapy for vulvar erosive lichen planus) was a feasibility study to assess if a definitive randomized controlled trial (RCT) of second-line systemic therapy for ELPV was possible.

Methods: 'hELP' was a multicenter, four-arm, open-label, pragmatic, pilot RCT. Randomized participants received a six-month course of hydroxychloroquine, methotrexate or mycophenolate mofetil, or a four-week reducing regimen of prednisolone (comparator group). The primary feasibility outcome was the proportion of eligible participants randomized. Secondary outcomes were the proportion of patients adhering to treatment, quality and suitability of clinical images, suitability of trial design and chosen clinical outcomes. The primary clinical outcome, measured at 6 months, combined patient global assessment and blinded assessment of images to determine 'success'.

Results: Over 14 months, 180 patients with ELPV were identified from 12 sites. Only 44/180 (24%) were eligible. The main reason for ineligibility was disease too mild (n=50). Of those eligible, 22/44 (50%) were randomized. Four participants did not start study medications, four stopped trial treatment early and two were lost to follow-up. Only 14/22 participants had complete before and after images, of which 10 were suitable for clinical assessment. Treatment success only occurred in the hydroxychloroquine (2/6, 33%) and mycophenolate mofetil (2/5, 40%) groups.

Conclusions: 'hELP' demonstrated reluctance to take systemic therapy and highlighted some specific limitations of a multi-arm study design. Better evidence is required on which to base treatment in this setting but, on the basis of these findings, a full-scale trial using this design did not proceed. It also emphasized the lack of suitable outcome measures available for vulvar disorders. To improve quality of vulvar skin trials in the future, core outcomes need to be agreed upon by the international community.

Stem Cell Enriched Lipotransfer as a Regenerative Treatment for Vulvar Lichen Sclerosus: Results of A Prospective Open Cohort Study

A Almadori^{1,2,3}, E Hansen⁴, A Bootle⁴, N Zenner⁵, D Boyle⁵, A Maclean⁵, W Reid⁵, and PEM Butler^{1,2,3}. ¹Department of Plastic Surgery, Royal Free Hospital, London, UK. ²UCL Centre for Nanotechnology and Regenerative Surgery, Division of Surgery and Interventional Science, University College of London, London, UK. ³Charles Wolfson Center for Reconstructive Surgery, Royal Free Hospital and University College of London, London, UK. ⁴Clinical Psychology, Department of Plastic Surgery, Royal Free Hospital, London, UK. ⁵Department of Gynaecology, Royal Free Hospital, London, UK.

Objectives: Lichen sclerosus is a chronic inflammatory condition that affects genital skin in the male and female. Recently, minimally invasive regenerative therapies including autologous fat transfer, adipose-derived stem cells (ASCs), or platelet-rich plasma (PRP) have been proposed as an additional option to treat the patients who are non-respondent to steroid treatment. The aim of the study was to evaluate the effect of lipotransfer in a cohort of women presenting with lichen sclerosus of the vulva.

Methods: A series of 20 prospective patients were treated with 1 to 2 autologous lipotransfers in the affected areas following enrichment through centrifugation. Standardized pre and post-operative assessments were used. These included clinical observation, photography, and a vulvar grading scale. Symptoms were measured with: 1) a validated visual analogic scale (VAS); 2) sexual function (female sexual function index); 3) sexual distress (female sexual distress scale); 4) psychological assessment (hospital anxiety and depression scale) and 5) intimacy (relationship assessment scale).

Results: The clinical score showed a significant improvement in all treated areas (p<0.05). A significant improvement was reported in the VAS for itching (p<0.05) and soreness (p<0.05). Sexual function was significantly improved after treatment (p<0.05), as was the distress associated with sexuality (p<0.05). The patients also reported a significant improvement in the level of anxiety (p<0.05) and depression (p<0.05).

Conclusions: Stem cell enriched lipotransfer is an effective treatment for vulvar lichen sclerosus. It reverses skin fibrosis, ameliorates the disease manifestations and patients' quality of life. Despite the encouraging results, further invitro studies and prospective clinical trials are required to better understand the mechanism of action and to confirm the efficacy and safety of this potentially transformative regenerative treatment.

In Office Surgery and Use of Platelet Rich Plasma for Treatment of Vulvar Lichen Sclerosus to Alleviate Painful Sexual Intercourse

LK Posey, MD¹, and C Runels, MD². ¹Private Gynecology Practice, Madisonville, LA, USA. ²Founder and Chairman at Institute for Lichen Sclerosus and Vulvar Health, Fairhope, AL, USA.

Objectives: To evaluate patients' symptoms and signs of vulvar lichen sclerosus and the ability to have pain free sexual intercourse after in office surgery to remove adhesions, followed by platelet rich plasma (PRP).

Methods: Fourteen patients with biopsy proven vulvar lichen sclerosus were seen in a private clinic between August 2014 and December 2016. All had some adhesions involving the clitoris, labia minora, and/or introitus. All experienced itching and pain. Of those who were sexually active, all had painful intercourse. The fourteen patients responded to a six-question survey, eight to ten weeks after initial treatment. The treatment consisted of in office surgery followed by PRP to the related sites. One provider performed all in office surgeries, as well as injections with PRP.

Results: All patients completed the questionnaire and recommended this treatment. Six patients were sexually active before treatment and nine patients after treatment. Four patients had no partner and one was gay. Of the sexually active patients, after treatment with surgery and PRP, 67% had sexual intercourse with no pain; 33% reported less pain. Of these same patients, 70% reported no bleeding; 30% reported less bleeding. The itching went away in 50% of all patients treated; improved in 43%; and no change in 7%. Ninety-three percent of the patients were happy with the treatment. Before and after photos of four of these patients are included in this abstract.

Conclusions: Patients reported improvement in their symptoms and signs of lichen sclerosus, including the ability to have pain free sexual intercourse. Surgery with PRP is an option to help improve the scarring associated with lichen sclerosus and decrease pain with sexual intercourse.





Vulvar Surgery in Young Women with Lichen Sclerosus and Dyspareunia or Apareunia

GM Rey Valzacchi, MD¹, C Marchitelli, MD², MC Sluga, MD³, G Secco, MD³, M Domenech, MD³, MS Peremateu, MD³, M Martinez, MD⁴, and S Gogorza, MD⁵. ¹Resident of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ²Chief of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ³Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁴Fellow of the Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ⁵Chief of Gynecology section, Hospital Italiano of Buenos Aires, Argentina.

Objectives: Lichen sclerosus (LS) is a chronic inflammatory condition, which affects the vulva. Many patients who report dyspareunia have introital stenosis on physical examination. Thus, patients have less frequent and less satisfying sexual activity than women without this disease. The objective of this study is to review the indications of surgery for introital stenosis related to vulvar lichen sclerosus, and to show its results.

Methods: The records of 11 patients who underwent surgery due to introital stenosis caused by LS in the Hospital Italiano of Buenos Aires were analyzed retrospectively. The mean follow-up period was 30 months (range, 6–84).

Results: The mean age of patients was 31 (18–46) years. The main complaints were dyspareunia, inability to achieve vaginal penetration, and urinary obstruction in three of the patients. In 10 cases, a perineoplasty was made. One patient refused perineoplasty and only lysis of adhesions was performed. Patients were able to initiate vaginal intercourse one month after surgery, with considerable relief of symptoms. 60% reported some degree of dyspareunia. One wound dehiscence was observed. Topical application of clobetasol propionate ointment and promestriene cream was continued post-operatively, and no relapses were detected.

Conclusions: Surgery is indicated in women with LS who experience sexual pain owing to anatomic changes and who wish to resume vaginal intercourse. In our experience, vulvar anatomy was restored with a low rate of surgical complications. While improved, resolution of dyspareunia may be incomplete. Discussion of sexual activities other than intercourse is essential. Maintenance with corticosteroids is also advised.

Genomic Profiling of Vulvar Lichen Sclerosus Patients Reveals Possible Pathogenetic Mechanisms of Disease

HK Haeflner, MD¹, K Welch, MD², AM Rolston, MD, MS¹, ES Koeppel, MS³, EM Stoffel, MD³, MJ Kiel, MD, PhD⁴, and MB Berger, MD, PhD¹. ¹Department of Obstetrics and Gynecology, Michigan Medicine, Ann Arbor, MI, USA. ²Department of Obstetrics and Gynecology, Wayne State University,

Detroit, MI, USA. ³Department of Internal Medicine, Michigan Medicine, Ann Arbor, MI, USA. ⁴Genomenon Inc., Ann Arbor, MI, USA.

Objectives: To explore the genetic profiling of patients with vulvar lichen sclerosus (VLS) to potentially uncover pathogenetic mechanisms, which may lead to improvements in targeted therapeutics or future areas of clinical research.

Methods: Whole exome sequencing (WES) was performed on seven patients affected by VLS from two unrelated families along with one unaffected paternal aunt from one pedigree. The results of WES were compared to population-specific allele frequency databases to prioritize variants likely to be contributing to VLS development.

Results: Recurrent germ-line variants in four genes were identified as likely to be deleterious to proper protein function in all of the seven probands and not in the unaffected control. The genes with variants included CD177 (neutrophil activation), ANKRD18a (ankyrin repeat protein), CD200 (inhibitory signal to macrophages), and LATS2 (co-repressor of androgen signaling). Studies are currently underway to determine the prevalence of these or similar variants impacting the same pathways in VLS patients generally. Although clinical significance of these genetic alterations is uncertain at this time, previous research suggests that neutrophil activation and macrophage inhibition may be related to granulomatous/autoimmune diseases, while Ankyrin repeat protein and co-repressor androgen signaling have been linked to tumor suppressor activities.

Conclusions: This is the first report to detail genetic profiling of VLS patients and may provide insight into the pathogenetic mechanism of this disease. Future research should focus on identifying whether these similarities are present in other affected families with VLS in order to better understand the pathophysiology of this condition in an effort to guide treatment.

Development of the Adult Vulvar Lichen Sclerosus Severity Scale—a Delphi Consensus Exercise for Item Generation

A Selk, MD^{1,2}, and M Sheinis, BSc^{2,3}. ¹Department of Obstetrics and Gynecology, Mount Sinai Hospital, Toronto, Ontario, Canada. ²Department of Obstetrics and Gynecology, University of Toronto, Toronto, Canada. ³Faculty of Medicine, University of Toronto, Toronto, Canada.

Objectives: To generate a list of items through international consensus for inclusion in a scale to measure the severity of adult vulvar lichen sclerosus.

Methods: This study was carried out as a three-stage Delphi consensus exercise. Following an extensive literature review, any items used to determine disease severity in previous clinical trials were compiled into a survey. The Delphi participants were recruited from the International Society for the Study of Vulvovaginal Disease (ISSVD). Participants were asked to rate the importance of items and in determining vulvar lichen sclerosus severity and were asked to indicate how these items should be measured. Consensus was defined as 75% agreement.

Results: Of approximately 400 members of the ISSVD, 66 participated in the study. Of the 14 symptoms presented, 7 reached consensus for inclusion (itch, pain unrelated to intercourse, pain with intercourse, bleeding and pain with intercourse, skin tearing with intercourse, quality of life, changes/decrease in sexual function). Of the 23 signs presented, 11 reached consensus for inclusion (fissures, whitening, crinkly/fine wrinkling of skin/parchment-like skin, extent of disease, erosions, ulcerations, hyperkeratosis, excoriations, lichenification, elasticity, sclerosis) and 1 reached consensus for exclusion (telangiectasia). Of the 6 architectural changes presented, all 6 reached consensus for inclusion (clitoral hood fusion, labial fusion/resorption, narrowing of the introitus, anterior changes, perianal involvement, and formation of posterior commissure bands/fourchette webs). No consensus was reached regarding method of measurement for any of the symptoms/signs.

Conclusions: International consensus was reached for a variety of signs and symptoms that should be included when assessing the severity of vulvar lichen sclerosus.

Co-existing Conditions in Patients with Lichen Sclerosus

RS Fowler, MD^{1,2}. ¹Consultant for Fowler Gyn International, PLLC Paradise Valley, AZ, USA. ²Emeritus Consultant in Gynecology, Mayo Clinic, Scottsdale, AZ, USA.

Objectives: To determine the frequency of co-existing conditions in patients with lichen sclerosus (LS).

Methods: Patient data between 7/1/07 and 7/1/12 with clinical signs of LS presenting to a Mayo Clinic practice specializing in vulvovaginal disorders were reviewed. The degree of LS was graded by the progression of clinical signs technique. Quantitative wet preparations were performed on vaginal secretions to determine the presence of coexisting conditions that could be implicated in vulvar symptoms.

Results: A total of 498 cases were reviewed. Lichen sclerosus was ranked severe in 95 (19%), moderate in 88 (17.7%), and mild in 315 (63.3%). Symptoms in decreasing order of frequency were itching (n=296 (59.4%)), burning (n=196 (39.4%)), a dry/chafed sensation (n=152 (30%)), cracks/paper cuts (n=152 (30%)), vaginal discharge (n=103 (20.7%)) and vaginal odor (n= 43 (9%)). Clinical signs of precancerous conditions were present in 17 (3.4%) with 7 (41%) of biopsies positive (1.4% of total patients). One-hundred ninety-one patients had burning without fissures plus vaginal discharge or odor. These symptoms are not attributable to LS. Of the 191, 158 (82.7%) had altered vaginal micro-flora patterns (32% of total).

Conclusions: Coexisting precancer is rare with in patients with lichen sclerosus. Patients with lichen sclerosus present with co-existing altered vaginal micro-flora.

Is Non-Response to Fluconazole Maintenance Therapy for Recurrent Candida Vaginitis Related to Host Immunity Disorders?

G Donders¹, S Grinceviciene², G Bellen², M Jaeger³, J ten Oever⁴, and MG Netea⁵. ¹Femicare Clinical Research for Women, Clinical Research for Women, Tienen, Belgium. ²Assoc. Femicare, Clinical Research for Women, Tienen, Belgium. ³Department of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, Netherlands. ⁴Radboud University Medical Center. ⁵Radboud University Medical Center, Nijmegen, Netherlands.

Objectives: Patients suffering from atopic disease and other autoimmune phenomena can develop recurrent vulvovaginal candidiasis (RVVC). We analyzed the relationship between failure to respond to maintenance fluconazole treatment for RCVV and the presence of immune-mediated disorders.

Methods: A prospective multi-center open label follow-up study, named ReCiDiF, was performed on women suffering from RCVV in ambulatory gynecology centers in Belgium. We analyzed the medical history, physical status, family history, and vaginal immune response of optimal and poor responders (N=71) to fluconazole maintenance treatment. We analyzed the results using Chi-square, Fisher exact, and Spearman rho tests, and compared means using the Mann-Whitney U test. We developed a multivariate logistic regression model and receiver operating characteristic (ROC) curve.

Results: Sociodemographic characteristics of 33 non-responding women were similar to those of 38 optimal responders. Responders with a score ≥ 3 on vulvar excoriation had a higher risk of non-response to therapy (OR = 3.99, CI 95% 1.41-11.23). Univariate regression analysis showed that family history of atopy (OR 3.61, CI 95% 1.17-11.18), and eczema (OR 5.76, CI 95% 1.13 – 29.44) were also related to non-response. Vulvar excoriation at entry was the only significant predictive factor for non-response in multivariate analysis with specificity 78.9% and sensitivity 54.0%.

Conclusions: Women with RCVV, who have family history of atopy and eczema, especially if presenting with severe vaginal excoriation, are at increased risk not to respond to maintenance fluconazole treatment. This finding is important for clinicians for predicting possible treatment outcomes.

The Mutable Profile of Infectious Candida Species and Resistance to Antifungal Agents: A Clinical and Laboratorial Study

LC Pereira^{1,3}, AF Correia^{2,3}, ZDL Silva³, CNR Oyama¹, L Gandolfi³, R Pratesi³, and YKM Nobrega³. ¹Department of Gynecology, Brasilia University Hospital, University of Brasilia, Brasilia-DF, Brazil. ²Central Laboratory, Health Secretariat of the Federal District (LACEN-DF), Parasitology and Mycology Center, Brasilia, DF, Brazil. ³Immunogenetic and Chronic-Degenerative Diseases Laboratory, School of Medicine, University of Brasilia, Brasilia-DF, Brazil.

Objectives: Identify candida species in patients with vulvovaginitis and determine their sensitivity to antifungal agents.

Methods: Eighty-four vaginal secretion samples of patients seen at the Brasilia University Hospital Gynecology outpatient clinic were analyzed. Nineteen patients were asymptomatic and 65 patients disclosed at least one of the following symptoms: vaginal discharge, vulvar hyperemia or edema, and localized itching or burning sensation. Candida phenotype was identified by culture, and confirmed by matrix assisted laser desorption ionization time-of-flight (MALDI TOF). The sensitivity profile of Candida species for fluconazole, voriconazole, amphotericin B, capsofungin and mycofungin was determined by the minimal inhibitory concentration (MIC).

Results: Sample analysis of the 65 symptomatic patients showed 73% (48) sensitivity, with 75% (36 of 48) of the phenotypes identified as Candida albicans, 22.9% (11 of the 48) as non-albicans species (respectively, 8.3% C. glabrata, 6.2% C. parapsilosis, 4.2% C. tropicalis, 2.1% C. krusei, 2.1% C. zeylanoides) and 2.1% (1 of 48) Rhodotorula mucilaginosa. C. albicans species were sensitive to all antifungal agents with the exception of one of the species that showed an intermediate sensitivity to amphotericin B (2.1%). Resistance was found among non-albicans species to fluconazole in 2.1% (C. glabrata), and to voriconazole in 2.1% (C. krusei).

Conclusions: In view of significantly increased infectivity of non-albicans species, with some phenotypes demonstrating resistance to usual antifungal agents, our results emphasize the need to precisely identify the Candida species to abrogate possible treatment failure and repetitive episodes of vulvovaginitis.

Reduced Antifungal Susceptibility of Vulvovaginal Candida Species at Normal Vaginal pH Levels: Clinical Implications

M Spitzer¹, and NP Wiederhold². ¹Hofstra Northwell School of Medicine, Departments of Pathology & Medicine/Infectious Diseases, Lake Success, NY, USA. ²University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.

Objectives: Antifungal susceptibility testing is routinely performed at pH 7 but the pH of the normal and yeast infected vagina is closer to 4. Our objective was to assess for differences in susceptibility at pH 7 and pH 4.

Methods: 310 yeast isolates were collected from 217 patients. The first isolates collected from each patient were included in the analysis. In patients who had more than one species cultured, the first isolate of each species was included. 173 C. albicans, 15 C. glabrata, and 29 from 8 other species first isolates underwent susceptibility testing at pH 7 and pH 4 against fluconazole, itraconazole, miconazole, clotrimazole, terconazole and nystatin.

Results: Geometric mean (GM) MICs for all antifungals were significantly higher when tested at pH 4 (p<0.001). For C. albicans, the largest GM MIC differences were observed for terconazole (0.17 pH 7 vs. 6.17 pH 4) and clotrimazole (0.04 vs. 0.24). For fluconazole, 5.2% of susceptible isolates at pH 7 (MIC<2) had MIC <4 at pH 4. For terconazole, 97.7% of the isolates had MIC<1 at pH 7 but 83.2% had MIC>4 at pH 4. For C. glabrata, terconazole (0.26 pH 7 vs. >64 pH 4), clotrimazole (0.13 vs. 6.96), miconazole (0.06 vs. 0.76) and fluconazole (3.17 vs. 26.60) were most affected. Nine of 15 C. glabrata isolates had MIC<2 for fluconazole at pH 7, but 14 of 15 had MIC>16 at pH 4. All C. glabrata isolates had MIC values of <1 for terconazole at pH 7, but one had MIC=8 and the other 14 were highly resistant (MIC>64) at pH 4.

Conclusions: Antifungals have reduced potency when tested at lower pH. C. glabrata is more affected than C. albicans. Although the clinical implication is unknown, the impact may be greatest for terconazole and C. glabrata.

Accuracy of DNA Probe Based Testing for Candida Vaginitis Compared with Office Microscopy

G Harris, MD¹ and LB Pinchover². ¹Saint Francis Hospital and Medical Center, Hartford, CT, USA. ²Sackler School of Medicine Tel Aviv, Israel.

Objectives: To compare DNA probe based testing using AFFIRM with office microscopy to diagnose Candida vaginitis. Comparisons were made regarding agreement of the two tests in diagnosing candida vaginitis, cost of the tool, and time delay until patients received results.

Methods: There were 89 patients who met the inclusion criteria. At the initial visit a 10% KOH and saline slide with vaginal secretions were examined under a phase contrast microscope. Positive testing was visualization of hyphae, spores, or mycelia. At the initial visit all patients had a sample sent for PCR testing using AFFIRM. PCR is the gold standard for diagnosis. Patients were contacted two weeks after the initial visit to assess resolution of symptoms. The Kappa test

score was calculated to determine agreement between microscopy and PCR testing. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using the PCR test as the gold standard.

Results: Kappa agreement between the PCR and microscopy was good (K=0.79, (0.66, 0.92)). There were 31 patients had both a positive microscopy and PCR. 47 patients had a negative microscopy and PCR for Candida. Eight patients had a positive microscopy and negative PCR, and 1 patient had a negative microscopy and positive PCR for Candida.

Conclusions: Our study supports use of microscopy as an initial tool to diagnosis Candida vaginitis in the office. Microscopy has lower cost, provides faster ability to treat symptomatic patients, and high concurrence to PCR testing.

Vulvar Melanosis: Clinical, Dermoscopic and Histologic Correlation and Approach To Management

D Ferrario¹. ¹Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: Vulvar melanosis and melanoma are particularly challenging clinical diagnoses, may result in patient and physician anxiety, and can lead to unnecessary, potentially disfiguring surgical procedures. We define the clinical, dermatoscopic and histopathologic characteristics of vulvar melanosis and propose an approach to its diagnosis and management.

Methods: A retrospective analysis of 5 patients with vulvar pigmented lesions with clinical diagnosis of suspected vulvar melanosis and/or melanoma was performed. Patient clinical records, clinical characteristics of pigmented areas, dermatoscopic features and histologic findings were evaluated for all pigmented lesions. All patients were referred to our Dermatology Department of the Italian Hospital of Buenos Aires, Argentina.

Results: The lesions varied in color, tan to dark brown/black, and size. In the detailed dermoscopic analysis we found: a ring-like pattern, structureless and globule-like patterns, a parallel pattern, as well as cobblestone-like, and reticular-like patterns. Histologic findings showed vulvar melanosis in all patients with increased melanin in the basal layer and a normal or slightly increased number of melanocytes arranged as single units at the dermoepidermal junction.

Conclusions: The diagnosis and management of vulvar melanosis should be based on a clinical and dermoscopic correlation to allow differentiation of vulvar melanosis from early melanoma. One or multiple biopsy specimens should be considered if the differential diagnosis between melanosis and melanoma cannot be made. Because vulvar melanosis is more commonly found among perimenopausal women, it is important that clinicians, dermatologists, and gynecologists carry out an adequate evaluation so as to avoid unnecessary treatments.

Vulvar Squamous Cell Carcinomas (VSCC). A 10- Year, Single Institution Review from The Hospital Italiano de Buenos Aires (HIBA)

M Saez-Perrotta¹. ¹Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: To examine clinical and pathological features of vulvar squamous cell carcinoma (VSCC) in a period of 10 years at our institution.

Methods: Patients diagnosed with VSCC between 2006 and 2016 were retrieved from the pathology files of the Hospital Italiano de Buenos Aires (HIBA). Clinical and pathologic diagnosis information were analyzed.

Results: A total of 52 VSCC were identified. 43 tumors (82%) were of conventional keratinizing type, 2 (4%) were non-keratinizing, 2 (4%) warty, 1 (2%) basaloid, and 4 (8%) verrucous type. Squamous intraepithelial lesions adjacent to VSCC were found in 36 (69%) cases, 12 (33%) were high-grade vulvar squamous intraepithelial lesions (HSIL) and 24 (67%) were differentiated vulvar intraepithelial neoplasia (dVIN). Within the group of patients with VSCC and HSIL, the mean age was of 62 years. 7 patients (58%) had multicentric HPV related lesions. No other vulvar dermatoses were found in the specimens nor in their previous clinical records. 4 (33%) were immunocompromised patients. 2 patients recurred, but none died of this disease. In the group of patients with VSCC with adjacent dVIN or with no HSIL, the mean age was of 74 years: 21 (53%) cases had no previous history of dermatoses; 7 patients had previous history of dVIN; 7 lichen sclerosus; 1 lichen simplex chronicus; and 1 vulvar acanthosis with altered differentiation. Only 1 patient had previous history of cervical HSIL. 16 (45%) patients recurred, and 9 of these died of this disease.

Conclusions: We report our experience in VSCC. 23% of our cases showed a link to HR-HPV pathway, and this group showed different clinical and pathologic history compared to the group with dVIN or no HSIL associated.

Immunomodulatory Treatment with Imiquimod 5% Cream in High-Grade Vulvar Squamous Intraepithelial Lesions

L Vallejos, MD¹, C Marchitelli, MD², MC Sluga, MD³, G Secco, MD³, A Wernicke, MD⁴, and S Gogorza, MD⁵. ¹Fellow of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ²Chief of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ³Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁴Pathology service, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁵Chief of Gynecology Section Hospital Italiano of Buenos Aires, Buenos Aires, Argentina.

Objectives: To evaluate the effectiveness and safety of imiquimod 5% cream for the treatment of high-grade squamous intraepithelial lesions (HSIL) of the vulva.

Methods: Retrospective cohort of 92 patients with a mean age of 47 years (23–72) with histopathological diagnosis of vulvar HSIL, treated with imiquimod 5% cream including mean follow up of 27 months (6–48) was performed. Patients applied imiquimod 3 times a week until total clearance of lesions or up to a maximum 6 months. Response was categorized as complete when there was no clinical evidence of lesions, partial when the area diminished >50%, and progressive when there was an increase of the lesion area. A biopsy was performed at the end of treatment and follow up was carried out monthly to evaluate adverse effects.

Results: Total clearance of lesions was observed in 54 of the 92 patients (58.69%) after 12–24 weeks. Twenty-eight patients (30.43%) had a partial response and 10 patients (10.86%) were non-responders; all of them received surgical treatment. No invasion was observed in the specimens. Eleven patients with complete response (11.95%) had recurrences during a mean of 27 months (6–48) follow-up. Of the 28 who had partial response, 5 were immunocompromised and 3 had poor adherence to treatment.

Conclusions: In this initial series, imiquimod proved to be an effective and less invasive for the treatment of vulvar HSIL compared to surgical options. The treatment was well tolerated; only local reactions were observed. Imiquimod represents a good alternative for the management of this disease.

Epidemiological, Clinical, Histological, and Immunohistochemical Aspects of Vulvar Intraepithelial Neoplasia Based on Five Cases

F Diaz-D'Aquaro, MD¹, C Perinetti, MD², J Pampillon, MD², M Maure, MD³, S Ciani, MD³, P Valdemoros, MD⁴, and E Farre, MD⁵. ¹Dermatology Department, Hospital Regional Diego Paroissien, Mendoza, Argentina. ²Gynecology Department, National University of Cuyo, Mendoza, Argentina. ³Pathology Department, Paroissien Hospital, Mendoza, Argentina. ⁴Pathology Department, Perupato Hospital, Mendoza, Argentina. ⁵Molecular Biology Laboratory, Mendoza, Argentina.

Objectives: To study the epidemiological, clinical, histological, and immunohistochemical characteristics of vulvar high-grade intraepithelial lesions (HSIL) and differentiated vulvar intraepithelial neoplasia (dVIN) at the Vulvar Pathology Section.

Methods: Clinical examination of patients age, smoking status, immunodeficiency history, and pathologic diagnosis of condyloma or neoplasia in the lower genital tract was performed. Tissue samples were analyzed to describe the histological patterns. We performed immunohistochemistry for p16 and p53 on the specimens.

Results: Out of the 5 patients with squamous intraepithelial lesions, 4 were HSIL and 1 was differentiated VIN. The 4 cases of HSIL included 1 basaloid and 3 warty variants. The average age of patients with vulvar HSIL was 49 years. 3 patients were former smokers and had a history of cervical HSIL. 1 patient developed invasive cervical carcinoma. 1 patient was immunocompromised from treatment for autoimmune hepatitis. The patient with differentiated VIN was 62 years old. Her histopathological analysis demonstrated lichen sclerosus adjacent to the lesion. At clinical examination, the 4 patients with vulvar HSIL had multifocal lesions, while the patient with dVIN had only 1 lesion. All cases of vulvar HSIL were positive for p16. Co-expression of p16 and p53 was found in 1 case. The case of dVIN was negative for p16 and positive for p53.

Conclusions: Two types of vulvar squamous intraepithelial lesions have been described. One is related to HPV infection and the other is not HPV-related but is associated with inflammatory dermatoses. Each type of squamous intraepithelial lesion has a different etiology, epidemiology, clinical and immunohistochemistry presentation.

Vulvar Basal Cell Carcinoma

SCAV Fialho, PhD^{1,2}, ICCV Guimarães, PhD¹, DSA Monteiro³, BO Vasconcelos³, JL Xavier³, L Pantaleão⁴, and GL Almeida Filho, PhD⁵. ¹Department of Maternal and Child Health, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ²Candidate for Fellowship, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ³Residents in Obstetrics and Gynecology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ⁴Department of Pathological Anatomy, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ⁵Instituto de Ginecologia, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil

Objectives: To report 3 cases of vulvar basal cell carcinoma.

Methods: A retrospective review of cases of vulvar basal cell carcinoma including three women, aged 75–81 years, referred to the Vulvar Pathology Service of the University Hospital Antônio Pedro (HUAP) of the Federal University of Fluminense (UFF) was performed.

Results: Three women, aged 75–81 years, were referred for solitary vulvar lesions, each around 5 cm, and large labia. In each case the clinical presentation was distinct: dark colored nodule, ulcerated nodule, and polychromic nodule. In each case a biopsy was performed with pathological confirmation of basal cell carcinoma. One included immunohistochemistry with positivity with BCL2 (focal), BER-EP4 and CK17 and negativity with EMA. All were treated with extensive lesion excision. They remain in follow-up at the HUAP Vulvar Pathology Service.

Conclusions: Basal cell carcinoma is the most common cutaneous malignant neoplasm in humans, mainly affecting individuals with light skin. The primary risk factor is exposure to ultraviolet radiation, being more prevalent in exposed regions. Only 2% of basal cell carcinomas occur on the vulva, affecting predominantly menopausal patients as was noted in our series. It corresponds to only 2% of the total cases of vulvar cancer, but should be considered among the differential diagnoses of vulvar lesions, which are often asymptomatic. Excision with clear margins of the lesion is the treatment of choice. Long-term follow-up is necessary because of the risk of local recurrence and onset of other primary cancers.



Vulvar Basal Cell Carcinoma: An Unusual Location

R Miloch, MD¹, C Marchitelli, MD², MC Sluga, MD³, M Martinez, MD⁴, and A Wemicke, MD⁵. ¹Clinical observer, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ²Chief of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ³Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁴Fellow of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁵Pathology service, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina.

Objectives: To present three cases of vulvar basal cell carcinoma (BCC), their histology, treatment and follow up.

Methods: We present three patients, aged 52 (image 1), 59 (image 2) and 65 (image 3), with a diagnosis of vulvar BCC, from September 2006 to June 2016, in our hospital.

Results: Three patients presented with pigmented lesions localized to the labia majora. All of them were asymptomatic. A biopsy was performed and the pathologic diagnosis was pigmented basal cell carcinoma. The surgical procedure consisted of resection of the lesions, with free margins of at least 5 mm. There were no recurrences after a mean follow-up of 5 years (2–8 years).



Conclusions: BCC is the most common cutaneous neoplasm in the white population. The main risk factor involved in its genesis is chronic sun exposure. The location in non-exposed areas is infrequent, less than 2%, and suggests the existence of etiological factors that are still unknown. The frequency of vulvar BCC is approximately 1%. The labium majus is the most frequent location. The pigmented variant described in the three cases presented is one of the less frequent histopathological varieties of this type of tumor. The growth of these lesions is slow and the frequency of metastasis is low, so an early diagnosis will allow adequate treatment with minimal impact on morbidity and mortality.

Clinicopathological Features of Vulvar Granular Cell Tumor

EV Greco, MD^{1,2}, A Fastuca, MD¹, and VC Grosso, MD^{1,2}. ¹Consultorio Privado de Ginecología y Obstetricia, Ciudad Autónoma Buenos Aires, Buenos Aires, Argentina. ²Consultorio de Patología, Los Polvorines, Malvinas Argentinas, Provincia de Buenos Aires, Buenos Aires, Argentina.



Objectives: Granular cell tumors (GCT) are infrequent soft tissue neoplasms that have been found throughout the body, including the female genital tract. They occur in both children and adults, with a higher incidence in the fourth to sixth decade. Most cases are benign. Malignant variants are described in 1-3% of cases. The vulvar involvement ranges from 5 to 16%. The purpose of this study was to review the clinicopathological features, surgical management and follow-up. **Methods:** We conducted a retrospective chart review of all patients that were diagnosed in a 15-year period (01/07/2001–30/06/2016). Three cases could be identified. Clinical data, histologic features, surgical treatment, and follow-up were reviewed.

Results: The median age was 52 years. The patients presented with a unique firm nodule located in the labia majora without pruritus or pain. The median tumor size was 2.3 cm. All cases were managed surgically with wide local excision. The samples were submitted for histopathological study with confirmation of vulvar GCT without malignant histological criteria and negative margins. The patients continue with annual gynecological exam as follow-up. Recurrence and metastasis have not been found.

Conclusions: We present 3 patients with GCTs confined to the labia majora as a firm nodule without other symptoms. The clinical diagnosis should include all vulvar masses. The histopathological diagnosis is mandatory but does not guarantee clinical behavior since there have been reports of malignant tumors retaining a benign histological appearance. The treatment of choice is wide local excision. The patient must be counseled to follow-up regularly with physical exams to detect recurrence, regional lymphadenopathy, or metastasis.

Invasive Vulvar Carcinoma and Lymphovascular Space Invasion: Presentation of Three Cases

V Maldonado, MD¹, R Caruso, MD¹, MC Eliseth, MD¹, L Fleider, MD¹, L Cardinal², and S Tatti, PhD¹. ¹Lower Genital Tract Unit, Division of Gynecology, Hospital de Clínicas Jose de San Martin, University of Buenos Aires, Buenos Aires, Argentina. ²Department of Pathology, Hospital de Clínicas Jose de San Martin, University of Buenos Aires, Buenos Aires, Argentina.

Objectives: To present three clinical cases of radical vulvectomy for vulvar squamous cell carcinoma (VSCC) with free margins and negative lymphadenectomy with inguino-femoral recurrence within 24 months.

Methods: Retrospective review of three patients with VSCC, mean age, 60 years. **Results:** The three patients underwent radical vulvectomy with bilateral lymphadenectomy. The three were stage II (FIGO 2009). Histopathology demonstrated squamous cell carcinoma with an average depth invasion 2 mm, free margins (1.5–3 cm), negative nodes, presence of lymphovascular space

invasion, and normal computed tomographic scan of the abdomen and pelvis. Inguinal recurrence occurred in 12 months average time. Mortality occurred within 24 months after the initial diagnosis for each.

Conclusions: We present 3 cases in which cancer recurrence occurred within the first two years. The presence of lymphovascular space invasion was present in each and may represent a prognostic factor for recurrence; consideration for adjuvant radiotherapy treatment may be indicated.

Verrucous Carcinoma versus Giant Condyloma of the Vulva: A 15 Years Retrospective Study

A Wernicke¹. ¹Department of Surgical Pathology, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina.

Objectives: The aim of the study was to assess the clinicopathological characteristics of patients with verrucous carcinoma (VC) and giant condyloma (GC) of the vulva.

Methods: We reviewed data on the age, disease course, pathologic diagnosis, treatment and follow-up of patients with VC or GC who were treated at our hospital during the past 15 years.

Results: Six cases of VC were identified. The mean age of patients was 65 years. Primary signs and symptoms were exophytic neoplasms with pruritus and/or pain. Surgical treatment included radical local excision and radical hemivulvectomy with inguino-femoral lymphadenectomy when invasion was found. Vulvar verrucous carcinoma occurred simultaneously with differentiated vulvar intraepithelial neoplasia (DVIN) in 3 cases, vulvar acanthosis with altered differentiation (VAAD) in 2 cases, and well-differentiated squamous cell carcinoma in 1 case. 2 patients with VC had a history of previous DVIN, and 1 patient had a history of VAAD. HPV testing was negative in 5 cases. The mean follow-up time period was 44.8 months. Local relapse developed in 2 cases (recurrence rate = 33%). None of the patients died of VC disease. Three cases of GC were identified; the mean age of these patients was 61. The primary signs were exophytic neoplasms. Surgical treatment included wide local excision and simple vulvectomy. GC was associated with a previous history of vulvar HSIL in all cases. p16INK4a (p16) by immunohistochemical staining was performed in all 3 cases of GC; all results were positive. The mean follow-up was 10 months with no recurrences.

Conclusions: Vulvar VC is a distinct type of slow-growing, nonmetastatic tumor with unclear etiology. These tumors should be distinguished from GC. Histological examination is the standard for diagnosis, although evaluation of HPV status may aid in the diagnosis. Surgery is the most effective treatment.

Verrucous Carcinoma of the Vulva: Report of Three Cases

F Gomez-Cherey, MD¹, V Suzuki, MD¹, MA Tinnirello, MD¹, L Kantorowicz, MD¹, F Garcia Kammermann², L Diaz, MD², and S Tatti, PhD¹. ¹Lower Genital Tract Unit, Division of Gynecology, Hospital de Clínicas Jose de San Martin, University of Buenos Aires, Buenos Aires, Argentina. ²Department of Pathology, Hospital de Clínicas Jose de San Martin, University of Buenos Aires, Buenos Aires, Argentina.

Objectives: To present three cases of verrucous carcinoma of the vulva.

Methods: Retrospective review involving three patients with verrucous carcinoma of the vulva.

Results: Three patients (mean age 63 years old) with initial diagnosis of squamous cell hyperplasia and suspicious lesions underwent local resection of the vulva with confirmation of invasive vulvar verrucous carcinoma and coexisting squamous carcinoma in two of the three cases. Subsequently, all patients underwent radical vulvectomy and inguino-femoral lymphadenectomy, with free margins and no involvement of lymph nodes. One patient had differentiated vulvar intraepithelial neoplasia two years later and had local excision. Another patient had recurrence of verrucous carcinoma and underwent radical surgery with chemotherapy. The third patient continues follow-up with no lesions.

Conclusions: Verrucous carcinoma represents a rare entity which most commonly presents in postmenopausal women. Surgery is considered the most appropriate treatment and its prognosis is relatively good. Recurrence occurs more frequently in patients with coexisting verrucous and squamous cells carcinoma.

Extramammary Paget's Disease of the Vulva (EMPD): A Novel Therapeutic Approach

MJ Martínez, MD¹, CE Marchitelli, MD², MC Sluga, MD³, DG Secco, MD³, MS Peremateu, MD³, MM Domenech, MD³, A Wernicke, MD⁴, and

S Gogorza, MD⁵. ¹Fellow of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ²Chief of the Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ³Center for Vulvar Disease, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁴Pathology service, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁵Chief of Gynecology section, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina.

Objectives: Vulvar Paget's disease is an intraepithelial adenocarcinoma which arises from the apocrine glands of the vulvar skin, representing 1-2% of vulvar cancers. It is typically diagnosed in women around 70 years of age and usually presents as a pruritic erythematous squamous lesion. Skin biopsy allows diagnosis, and immunohistochemistry has a key role in differentiating primary and secondary disease. Treatment consists of surgical excision; local recurrence rate is high. The objective of this study is to describe 24 cases of extramammary Paget's Disease (EMPD) of the vulva and compare clinical pathological characteristics and management.

Methods: Observational retrospective study including patients with vulvar EMPD who were followed at the Hospital Italiano of Buenos Aires between June 2006 and June 2016.

Results: The mean age at presentation was 71.2 years. In 23 cases, primary EMPD was the diagnosis and one patient presented with EMPD associated with urothelial carcinoma. Among the 23 cases of primary EMPD, 20 had intraepithelial disease and 3 had invasive disease. Eleven patients underwent primary surgical treatment. Six of the 11 patients presented local recurrence and were treated with 5% topical imiquimod, of whom 5 had complete clinical response. The remaining 13 patients received primary imiquimod treatment, achieving complete response in 7 cases. Clinical resolution was attained after an average of 5 months of treatment. Post-treatment biopsy was performed in all patients with complete clinical response for confirmation of concomitant complete pathologic response. The mean follow-up was 39 months.

Conclusions: Based on our study, we propose 5% imiquimod cream as a valid alternative for the treatment of primary and recurrent vulvar EMPD. It proved to be a safe and effective option, especially in those patients with extensive lesions or those at high risk for surgical treatment because of comorbidities.

Vulvar High-grade Squamous Intraepithelial Lesions in Elderly patients

M Peremateu¹, C Marchitelli, MD², M Domenech¹, C Sluga¹, M Florencia Marcos¹, G Secco¹, A Wernicke¹, and S Gogorza¹. ¹Department of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ²Chief of Center for Vulvar Disease, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: Vulvar high-grade squamous intraepithelial lesions (HSIL) are commonly detected in young women, smokers, and immunosuppressed, with a history of several sexual partners. However, in the last few years, it has been diagnosed in women older than 60 years, without the mentioned risk factors. We intended to evaluate whether recent sexual contact is a necessary cause for the development of vulvar HSIL and to confirm the presence of these HPV lesions using histological criteria and immunohistochemistry (IHC) (p16) as a diagnostic tool, correlating it with the results of polymerase chain reaction (PCR).

Methods: We conducted a retrospective analysis of data collected from electronic medical records of patients referred to the vulvar section of the Hospital Italiano de Buenos Aires, who were diagnosed with vulvar HSIL, between October 2006 and March 2017. Information about risk factors as well as diagnostic methodology and biomarker results was obtained.

Results: 26 patients over 60 years old were included, but only 14 (53.8%) who did not have sex at least 10 years prior to the diagnosis were analyzed and found to have HPV. The mean age of this group was 73.8 years old (61–87). None were smokers or immunosuppressed.

Conclusions: The presence of related HPV vulvar lesions was demonstrated in patients without recent sexual contact. This may be due to reactivation of the virus acquired decades ago and not to a new sexual exposure. Histology remains the key to the diagnosis of this entity, with the IHC as a confirmatory tool.

Vulvar Squamous Cell Carcinoma: Clinical, Histological, and Immunohistochemical Characteristics

C Perinetti, MD¹, J Pampillon, MD¹, F Diaz-D'Aquaro, MD², M Maure, MD³, S Ciani, MD³, P Valdemoros, MD⁴, C Monge, MD⁵, and E Farre, MD⁶. ¹Gynecology Department, Paroissien Hospital, Mendoza, Argentina. ²Dermatology Department, National University of Cuyo, Mendoza, Argentina. ³Pathology Department, Paroissien Hospital, Mendoza, Argentina. ⁴Pathology Department,

Perrupato Hospital, Mendoza, Argentina. ⁵Departement Pathology, Italian Hospital, Mendoza, Argentina. ⁶Molecular Biology Laboratory, Mendoza, Argentina.

Objectives: To analyze the histopathology of vulvar squamous cell carcinoma and their clinical and immunohistochemical characteristics.

Methods: We analyzed data for 21 patients diagnosed with invasive vulvar cancer between 2009 and 2015. 15 cases of squamous cell carcinoma (SCC) were included in the study. Histology samples were analyzed for histologic type, associated lesions, depth of invasion, growth pattern, tumor grade, and vascular/lymphatic and lymph node involvement. All samples were immunolabeled for p16 and p53. Patients' treatment and their epidemiological and clinical history were also assessed.

Results: For these 15 SCC patients, SCC subtypes were classified as warty (5), basaloid (2), and keratinizing (8). All tumors were G2, except for 3 warty cases that presented G1. At the time of diagnosis, 9 patients were stage I/II and 6 were stage III/IV. Depth of invasion was <6mm for all warty subtypes and >7mm for keratinizing subtypes (11.7 mm on average). 6 out of the 7 patients with warty and basaloid SCC presented vulvar HSIL close to the invasive lesion. Out of the 8 patients with keratinizing-SCC only 3 presented areas of differentiated-VIN and 5 were diagnosed with lichen sclerosis. p16 overexpression was observed in all warty and basaloid subtypes (7), which were associated to stages I and II, node-negative disease and expansive growth pattern. p53 expression was observed only in 2 keratinizing-SCCs that also presented an infiltrative growth pattern and deeper invasion. There were 11 radical vulvectomy/hemivulvectomy and 6 lymphadenectomies. The sentinel node was identified in 9 patients. Cutaneous flaps were used in 7 patients for reconstruction purposes. 10 patients received adjuvant radiotherapy.

Conclusions: The histologic subtypes of vulvar SCC present different features and specific behavior. The immunohistochemical profile can be very useful in the diagnosis, assessment, and treatment of SCC patients.

"Premalignant and Malignant Lesions of Cervix in Patients with Vulvar Condylomatosis who Attended the Pathology Service of Lower Genital Tract of the Obstetrics Gynecology Isidro Ayora Hospital from January to February Of 2017"

L. Salto¹ ¹Especialista en Ginecología y Obstetricia, Área de Patología del Tracto Genital Inferior, Hospital Gineco Obstétrico Isidro Ayora, Quito, Ecuador.

Objectives: To determine the prevalence of premalignant and malignant lesions of the cervix in patients with vulvar condyloma who presented to the Pathology Service of Lower Genital Tract of the Obstetrics Gynecology Isidro Ayora Hospital from January to February of 2017.

Methods: Observational Descriptive Study of transversal cut in 20 women who attended the Pathology Service because of vulvar lesions.

Results: Twenty patients were observed: average age was 31.15 years, average age at the beginning of sexual life was 19.15 years, and the average number of sexual partners was 1.6. Fourteen patients were using family planning/contraception: hormonal methods in 6 and non-hormonal methods in 8 cases. Additionally, the majority did not smoke, with tobacco use in only 1 case. The vulvar condylomas were studied by histopathology in all cases. Cervical low-grade intraepithelial lesions were identified in 2, and high-grade intraepithelial lesions in 1 cytology. The colposcopy was grade 1 in 13 patients and grade 2 in 2 patients. The histopathological study demonstrated 10 low-grade lesions (50% of the cases) and 2 high-grade lesions.

Conclusions: There exists a high prevalence of premalignant and malignant cervical lesions in patients with vulvar condyloma.

Perception of Sexuality in Patients with Vulvar Warts

A Garcia, MD¹, F Ceragioli, MD¹, S Sanguino, MD¹, M Avalle, MD¹, and M Ledesma, MD^{1,2}. ¹Rawson Hospital, Department of Lower Genital Tract, Cordoba, Argentina. ²Chief of Gynecology of Rawson Hospital, Cordoba, Argentina.

Objectives: This study was aimed at determining the impact of having a diagnosis of HPV regarding sexuality in women with vulvar warts.

Methods: A case series was done in patients with warts diagnosed at the Inferior Genital Tract Department of Rawson Hospital in the city of Córdoba (Argentina). Patients were enrolled from December 2016 to January 2017. Inclusion criteria were current diagnosis of vaginal, vulvar, or anal warts and ability to complete the changes in sexual functioning questionnaire (CSFQ)-14 (the validated Spanish short form). The statistical analysis was done in statistical

package for the social sciences (SPSS), analysis of means for continued variables and univariate for categorical variables.

Results: We included 14 patients aged from 18 to 48 years. The mean age of sexual initiation was 16 years and the mean number of sexual partners was 5 (table 1). 85% of the sample claimed to be in a stable relationship. 41% of the patients had HIV and 30% were smokers. The vulva was the most common location of warts. 57% of patients were not having sexual relations due to the presence of warts. From this group, 37.5% had the feeling of shame or discomfort, 12% had fear of infecting others, 12.5% per partner request, 25% due to the pain of the lesions, and 12% for other causes. Question number 2 (sexual intercourse frequency) and number 11 (orgasm frequency) were analyzed (table 2).

CSFQ-F® Questions	MODE
2- How frequently do you engage in sexual activity now?	4
3- How often do you desire to engage in sexual activity?	3
11- How often do you experience an orgasm?	3
	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always

N=14	AGE	AGE OF SEXUAL INITIATION	NUMBER OF SEXUAL PARTNERS	PREGNANCY
MEAN	25.93	16.64	4.93	1.14

Conclusions: This case series suggests that the diagnosis of warts modifies the perception of sexuality and the sexual behavior in patients who suffer from this condition.

Cosmetic Surgery Committee-Position

P Vieira-Baptista¹, G Almeida², F Bogliatto³, T Boh¹, M Burger², B Cohen-Sacher⁶, K Gibbon⁸, A Goldstein⁸, D Heller⁹, W Likes¹⁰, C Longo-da-Silva¹¹, C Marchitelli¹², M Moyal-Barraco¹³, K Posey¹⁴, MC Sluga¹², C Stockdale¹⁵, G Vissoci Marquini¹⁶, and K Zalewski^{17,18}. ¹Lower Genital Tract Disease Unit, Centro Hospitalar de São João, Porto, Portugal. ²Institute of Gynecology, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil. Post-Graduate Program in Surgical Sciences, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil. ³Lower Female Anourogenital Tract Network - ASLTO4, Chivasso Civic Hospital, 10034 Chivasso, Torino, Italy. ⁴Vulva Clinic, Jean Hailes Medical Centre, Clayton, Victoria, Australia. ⁵Emeritus professor of Gynaecology, University of Amsterdam, The Netherlands. ⁶Department of Obstetrics and Gynecology, Helen Schneider Hospital for Women, Rabin Medical Center, Petach Tikva, Israel. ⁷Department of Dermatology, Barts Health NHS Trust, London UK. ⁸The Center for Vulvovaginal Disorders, Washington, DC, USA. ⁹Department of Pathology, Rutgers-New Jersey Medical School, Newark, NJ, USA. ¹⁰Dean and Professor, College of Nursing, University of Tennessee Health Science Center, Memphis, TN, USA. ¹¹Faculdade de Medicina da Universidade Federal de Pelotas, Brazil. ¹²Chief of Vulvar Department, Department of Gynecology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. ¹³Department of Dermatology, Hôpital Tarnier-Cochin, Paris. ¹⁴Private Practice, USA. ¹⁵Department of Obstetrics & Gynecology, University of Iowa, Iowa City, Iowa, USA. ¹⁶Gynecology and Obstetrics, Nucleus of Health Assistance to the Worker, Federal University of Uberlandia, Minas Gerais, Brazil. ¹⁷Department of Gynecologic Oncology, Holycross Cancer Center, Kielce, Poland. ¹⁸Chair and Department of Obstetrics, Gynecology and Oncology, 2nd Faculty of Medicine, Warsaw Medical University, Poland.

The number of vulvovaginal cosmetic surgeries and procedures is increasing worldwide, despite the lack of scientific evidence supporting either the need for many of these or their efficacy. These are being offered and advertised as common, simple and complication-free procedures, capable of not only improving aesthetic appearance, but also increasing self-esteem and enhancing sexual pleasure for both women and their partners. Complex social factors are actively creating a perceived problem/disease for which surgical intervention is being offered as a cure.

This committee reached a consensus in the following points:

1. There is a wide variation in terms of normalcy of the look of the genitals; physicians must be able to explain this to women.
2. All women undergoing cosmetic genital surgery should previously be evaluated by a gynecologist; attention must be paid to their psychological and social context. Evaluation by a mental health provider should be considered when the motivation for seeking surgery and/or expectations are not clear or realistic.
3. Women should not be submitted to labiaplasty before adulthood.
4. There are no data supporting the performance of hymenoplasty, vulvar bleaching/whitening, vaginal tightening procedures, G-spot augmentation and other procedures aimed at increasing sexual function.
5. Cosmetic genital surgery is not exempt from complications.
6. A thorough informed consent must always be obtained.
7. Surgeons performing cosmetic genital surgery should refrain from solicitous advertising or promoting procedures without scientific basis, including on websites.
8. Surgeons must resist patient's pressure to perform surgeries that they do not agree with and explain their rationale/position.
9. The surgeon must be adequately trained and experienced in performing the surgery and have knowledge of the anatomy, physiology and pathophysiology of the vulva, vagina and adjacent organs.

Guidelines for physicians and clear, scientifically correct information for patients must be made available, in order to minimize the number of ineffective or even deleterious interventions in this area.

Talking to Patients about Sexuality: What the Vulvologist Needs to Know

C Piper, LMSW¹. ¹University of Michigan Sexual Health Certificate Program, University of Michigan School of Social Work, University of Michigan, Ann Arbor, Michigan, USA.

All women will likely experience some type of sexual change, difficulty, or dysfunction during their lifetime. Due to the symptoms that accompany vulvar disease, these patients are particularly vulnerable to sexual concerns. However, both patients and medical professionals find sexuality difficult to discuss. Lack of discussion can lead to patient and partner distress, incomplete reporting of medical symptoms and possible treatment non-compliance. Because sexual functioning is much more than a physiological experience, but is heavily influenced by psychological, relational, and cultural factors, clinicians must use a bio-psycho-social lens, rather than the traditional biomedical lens, to sensitively understand and assess the full extent of their patients' sexual concerns. This multidimensional approach informs the "who, when, how and what" of a sexual health assessment integrated into the medical assessment. A basic understanding of the delineation of sexual dysfunction according to the DSM 5 (Diagnostic and Statistic Manual) and ICD 10; sexual identity and orientation issues; complexities of relationship dynamics; and the sequelae of physical, emotional or sexual trauma are important to skillful sexual health assessment and treatment. In addition, multidisciplinary collaboration and timely referral for psychological, couple, and/or sex counseling is a valuable and necessary adjunct to medical treatment.

Core Outcome Set Development for Vulvovaginal Disease

DC Foster, MD, MPH¹. ¹The University of Rochester, Rochester, NY, USA.

Clinical trials in medical research have been criticized for lack of reproducibility, for difficulty in cross-comparison of studies, and for lack of clearly defined, well-validated, reliable, and responsive outcome measures. No group of women's health conditions calls for greater improvement in research methods than chronic vulvovaginal disorders, one of the most common ambulatory care complaints frequently associated with chronic pain and sexual dysfunction. Ironically, clinical research in chronic vulvovaginal disorders has lagged behind other women's health disciplines in terms of funding availability and overall volume of high-quality clinical research. Independently developed workgroups, diverse in focus, and geographic location, have begun to address improved research in vulvovaginal disorders. However, the various workgroups lack a unifying focus. It is our intention, under the auspices of two major professional societies, ASCCP and the ISSVD, to provide overall direction, organize a venue for expert panel consensus meetings on outcomes measures, and facilitate publication of consensus results. The vulvovaginal Core Outcome Set (COS) initiative will remain relatively broad in scope, covering a spectrum of at least

three large disease categories: 1) vulvovaginal pain, 2) vulvar inflammation/dermatoses, and 3) vulvovaginal infections/chronic discharge. Future consensus meetings will cover the disease categories and focus on three major goals: 1) Delimiting clinical conditions within each disease category and identifying core domains within each condition, 2) Identifying and defining core outcome measure instruments within each domain, and 3). Develop networks on which to base future collaborative randomized clinical trials (RCT's) in the respective disease states. Publication of internationally accepted core outcome measures for clinical trials would enable the synthesis of evidence-based practice and facilitate cross-comparison and meta-analysis of studies.

Workshop: "Clinical Research in Vulvar Disease: A Multidisciplinary Approach"

M Halac, MD¹, R Iannantuono, MD², M Prada, MD³, and D Salmun, MD⁴. ¹Department of Cardiology, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ²Foundation of Pharmacological Studies and Medications (FEFyM), Buenos Aires, Argentina. ³Department of Gynecology, Hospital Italiano of Buenos Aires, Buenos Aires, Argentina. ⁴ANMAT- Ministry of Health, Argentina. Workshops's main objectives:

- i) To approach and discuss the ethical, legal, and operative framework for clinical research in vulvovaginal disease, focusing on the particular features of the disease and the study population.
- ii) To encourage and fortify the Research capacities of all professionals and non-professionals involved in the ISSVD's study topics.

Pivotal points to be covered:

i) Theoretical - conceptual framework of Clinical Research in Vulvar Disease:

- Who should participate in vulvar and vaginal clinical research, how to do it, why and what for?
- Research capacities in women's health. Acquiring generalizable knowledge while protecting human research participants.
- Highlights on CIOMS 2016- International Ethical Guidelines for Health-related Research Involving Humans.
- Clinical Research in vulnerable persons and populations: Women as clinical research participants.

ii) Clinical Research Sites:

- Organize a site in a proper way in order to provide high quality clinical research standards, applying regulations for rights' protection, safety and welfare of human subjects.
- Identify human and technical resources needs to participate in clinical research and take full responsibility for the proper conduct of the study.

iii) Site operative approach: Clinical research from the investigator's point of view:

- How to obtain valuable information, while protecting and respecting your patients?
- What does it mean in practical terms?
- Investigator responsibilities before initiation, during conducting and following the completion of trial.
- Interactions between the investigator and other actors involved in the trial.
- Site organization: training, patient selection, visits, procedures, CRF.
- Investigator reports. Essential documents.
- Trial Master file/Investigator Site File, etc.

iv) Informed consent as:

- a) Requirement to satisfy the ethical principle of autonomy.
- b) Investment instead of bureaucratic procedure.

A fundamental tool to generate and/or strengthen the patient researcher relationship.

Update: Vulvar Squamous Intraepithelial Lesions

M. Preti¹, L. Micheletti¹, and L. Bucchi². ¹Department of Obstetrics and Gynaecology, University of Torino, Torino, Italy. ²Romagna Cancer Registry, Romagna Cancer Institute (IRST) IRCCS, Meldola, Forlì, Italy.

Epidemiological data are consistent with an increased incidence rate of invasive vulvar squamous cell carcinoma (VSCC) in women less than 50 years. Unfortunately, unlike cervical disease, there is no screening for Vulvar Highgrade Squamous Intraepithelial Lesions (HSIL) that can only be suspected and biopsied during the visual assessment of the vulvar region.

High-resolution dermoscopy has been suggested as a complement of clinical examination, providing an adjunctive tool to biopsy suspected vulvar HSIL, taking into account that unrecognized invasive carcinoma is reported in more than 10% of patients undergoing surgical excision after an office biopsy of vulvar HSIL.

The 2015 ISSVD terminology for vulvar HSIL represents a cornerstone to underline the dual etiology of VSCC precursor lesions and to ask to clinician and pathologists the best efforts to diagnose them.

Studies on HPV type specific distribution, integrated with studies assessing peripheral and in situ lymphocyte function during HPV persistence in vulvar HSIL might play an important prognostic role in identifying the risk of progression in HPV-driven vulvar cancer.

Compared with vulvar HSIL, differentiated Vulvar Intraepithelial Neoplasia (dVIN) is a more rapidly progressing precursor, that does not show p16ink4a overexpression but often reveals TP53 mutations.

Findings on activating mutations in PI3K/AKT/mTOR pathway underline that researches are needed to identify and treat precursor lesions with mutations that can drive HPV-unrelated carcinogenesis.

On the other side - exploration of the safety, tolerability and clinical efficacy of therapeutic HPV vaccines that eliminate HPV transformed cells is one of the greatest challenges for gynecological oncology.

Morphological Vaginal Changes in Cervical Cancer Survivors Affecting Sexual Health

Alexandra Hofsjö¹, Bo Blomgren², Karin Bergmark³, Nina Bohm-Starke⁴. ¹Department of Oncology-Pathology, Karolinska Institutet, and Unit of Gynecological Oncology, Radiumhemmet, Karolinska University Hospital, Stockholm, Sweden. ²Department of Clinical Sciences, Karolinska Institutet, and Department of Pathology, Karolinska University Hospital, Stockholm, Sweden. ³The Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden. ⁴Department of Clinical Sciences, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden.

Objectives: Women who have been treated for cervical cancer have persistent changes in their sexual function, which result in considerable distress. Advances in treatment have resulted in improvement in survival rates and a rising number of cervical cancer survivors. Still, the morphology of the vaginal wall after treatment with radiotherapy and its role in sexual health is unknown. The objective was to investigate the vaginal morphology in cervical cancer survivors treated with radiotherapy.

Methods: We included 34 patients treated for cervical cancer with radiotherapy and 37 healthy age-matched controls. The patients were treated with radiotherapy with or without surgery and/or chemotherapy. Vaginal biopsies were obtained and analyzed by epithelial morphometry and analyses for elastin and collagen content. Clinical examination was performed for estimating atrophy, amount of telangiectasia and pelvic fibrosis. Questionnaires were used for psychosexual evaluation.

Results: The cancer survivors had marked morphological vaginal changes compared to controls. The epithelial measurement showed atrophy as reduced epithelial volume. Elastosis was found in the connective tissue with altered distribution of the elastin fibers. The collagen fibers were of high density and clinical examination showed different degrees of atrophy, telangiectasia, and pelvic fibrosis. Report of physical sexual dysfunction with reduced vaginal elasticity at intercourse, reduced lubrication, and dyspareunia were common.

Conclusions: Women who have been treated with radiotherapy for cervical cancer have morphological changes in the vaginal wall with atrophy and fibrosis as the predominant findings. Early use of topical estrogen and dilators may improve the sexual function in the survivors.

Vulvar Lichen Planus is not Associated with Squamous Cell Carcinoma

T Day, MD¹², G Otton, CGO³ K Jaaback, CGO³ J Weigner⁴, and J Scurry, FRCPA¹⁴. ¹Faculty of Health and Medicine, University of Newcastle, NSW, Australia. ²John Hunter Hospital, Division of Gynecology, Newcastle, NSW, Australia. ³Division of Gynecologic Oncology, John Hunter Hospital, Division of Gynecology, Newcastle, NSW. ⁴Pathology North, Hunter New England, Newcastle, NSW, Australia.

Objectives: To determine the incidence of vulvar lichen planus (LP) with non-human papillomavirus (HPV)-related squamous cell carcinoma (SCC).

Methods: We performed a clinicohistopathologic review of consecutive vulvotomies and wide local excisions for non-HPV related vulvar or vaginal SCC from 2007 to 2016. Clinical data collected included tumor location and dermatologic diagnosis and treatment. Histopathological review included site of SCC, adjacent precursor lesions, and dermatoses.

Results: There were 39 first presentations of primary non-HPV related vulvar SCC treated by excision, but no cases of primary non-HPV related vaginal cancer. 22 (56%) women had a clinical diagnosis of lichen sclerosus (LS); none had a diagnosis of LP. Topical steroids were prescribed intermittently in 16 (41%) and as a long-term maintenance regimen in 2 (5%). Tumors arose from the labia minora, labia majora, and clitoral region, but not from vestibule or perianus. On histopathological review, LS was present in 38/39 (97%) and there was 1 non-specific lichenoid reaction on hair bearing skin. No erosive, hypertrophic, or typical LP was seen. Differentiated vulvar intraepithelial neoplasia (dVIN) was present in 34/39 (87%), 1 had acanthosis with altered differentiation, and 4 (10%) had no precursor lesion. dVIN had areas of basaloid morphology superficially resembling erosive LP in 9 (26%), and had a similar appearance to hypertrophic LP in 3 (9%).

Conclusions: LP was not seen in association with non-HPV related vulvar SCC, while LS is under-recognized and inadequately treated in this group. Pathologists need to be aware that dVIN may resemble erosive or hypertrophic LP.

Vulvar High-Grade Squamous Intraepithelial Lesion (HSIL): Risk Factors for Recurrence after Excisional Therapy

W Satmary, MD¹, L Brunette, MD⁴ S Natarajan⁵ and CH Holschneider, MD²³. ¹Department of Obstetrics & Gynecology, Kaiser Permanente Medical Center, Panorama City, CA, USA. ²Department of Obstetrics & Gynecology, Olive View-UCLA Medical Center, Sylmar, CA, USA. ³David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. ⁴LAC+USC Medical Center, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA. ⁵Department of Pathology, Kaiser Permanente Medical Center, Los Angeles, CA, USA.

Objectives: To identify risk factors associated with recurrence of vulvar high grade squamous intraepithelial lesions (HSIL) following excisional therapy.

Methods: We performed a retrospective cohort study of women who underwent excisional therapy for a histologic diagnosis of HSIL of the vulva (vulvar intraepithelial neoplasia (VIN) 2/3/carcinoma in situ) within Southern California Permanente Medical Group between 1995-2007. Terms HSIL and differentiated-type VIN (dVIN) were not used during our study's timeframe; women with VIN 1, or low-grade squamous intraepithelial lesion (LSIL), were excluded. Medical records/pathology were reviewed to determine potential demographic, medical and pathological risk factors for recurrence. Statistical analyses included Chi-squared and Student's t-tests, cumulative incidence analysis, univariate and multivariate logistic regression.

Results: Among the 418 patients who underwent excisional treatment alone, median age was 50.1 years; 69% were white, 13% Hispanic, and 10% black. Margins were positive in 204 (48.8%) and negative in 214 (51.2%). Median follow-up was 89 months. 104 women had recurrence (25%). Of those with positive margins, 41.7% recurred compared to 8.9% with negative margins ($p < 0.0001$). Median time to recurrence was 14.3 months for patients with positive margins and 41.8 months for those with negative margins. Significant risk factors for recurrence in multivariate analysis included positive margins (OR, 8.165; 95% CI 4.595 to 14.509), lichen sclerosus (LSA) (OR, 6.914; 95% CI 1.526 to 31.320) or HPV changes (OR, 2.152; 95% CI 1.259 to 3.680) on adjacent pathology, and immunosuppression (OR, 1.949; 95% CI 1.127 to 3.370). Cumulative-incidence analysis revealed that women with positive margins remain at increased risk for recurrence compared to those with negative margins not only early following treatment (14% vs. 1.4% in first 6 months) but also long-term (26.1% vs. 7.4% post 24 months of follow-up).

Conclusions: Positive margins and VIN-adjacent to lichen sclerosus are the strongest predictors of recurrence after excision of HSIL. Patients with positive margins are at increased risk for both, early and delayed recurrence and require close long-term surveillance.

Vaginal and Vulvar Intra-Epithelial Neoplasia in Young Women Attributed to 14 Human Papillomavirus Genotypes

M Steben, MD¹. ¹STI unit, INSPQ and Clinique A, Montréal, Canada.

Objectives: To estimate the proportion of vulvovaginal lesions in young women attributable to human papillomavirus (HPV) types preventable by the 9vHPV vaccine.

Methods: Prospectively diagnosed vulvar and vaginal low- and high-grade squamous intraepithelial lesions (LSILs and HSILs, respectively) among 8,798 women 15–26 years old enrolled in the placebo arms of two phase 3 randomized HPV-vaccine trials. They were analyzed for the presence of 14 HPV genotypes (6/11/16/18/31/33/35/39/45/51/52/56/58/59).

Results: Overall, 40 vulvar LSILs, 46 vulvar HSILs, 118 vaginal LSILs, and 33 vaginal HSILs were detected with approximately 4 years of follow-up. At least one of the 14 types were detected in 72.5%, 91.3%, 61.9%, and 72.7% of these lesions, and multiple HPV types were detected in 40.3%, 30.4%, 24.1%, and 45.2% of the HPV-positive lesions, respectively. After accounting for co-infections, 60.0–67.5% of vulvar LSILs, 76.1–91.3% of vulvar HSILs, 27.1–43.2% of vaginal LSILs, and 42.4–60.6% of vaginal HSILs were attributable to 9vHPV vaccine types. Among the HPV-positive lesions, 89.4% of vulvar LSILs, 100% of vulvar HSILs, 56.0% of vaginal LSILs, and 78.3% of vaginal HSILs were attributable to 9vHPV vaccine types, accounting for 1.7% of vulvar LSILs, 16.1% of vulvar HSILs, 30.8% of vaginal LSILs, and 20.9% of vaginal HSILs (Table).

Conclusions: Widespread uptake of the 9vHPV vaccine could potentially prevent a sizeable fraction of benign and precancerous HPV-related vulvar and vaginal lesions.

Table. Proportionally weighted percentages of potentially vaccine-preventable HPV-positive vulvovaginal lesions.

Vaccine	2vHPV	4vHPV	9vHPV	None ^a	
Targeted HPV genotypes ^b	16/18	6/11/16/18	6/11/16/18/31/33/35/52/58	35/39/51/56/59	
Vaginal	LSIL	18.8%	25.2%	56.0%	44.0%
	HSIL	53.1%	57.4%	78.3%	21.7%
Vulvar	LSIL	10.7%	87.7%	89.4%	10.6%
	HSIL	74.3%	83.9%	Up to 100.0%	0.0%

^aA total of 14 HPV types were assessed. Some lesions not categorized as HPV-related could have been caused by other HPV types for which genotyping was not performed. Some HPV types not genotyped could have been present in lesions categorized as HPV-related.
^bNot covered by any of the 3 vaccines.

Epidemiology of Anogenital Warts in a Group of Argentinian Women and the Impact on their Quality of Life

V Suzuki, MD¹, V Maldonado¹, M Tinnirello¹, F Gomez Chery¹, L Kantorowicz¹, and S Tatti¹. Hospital de Clínicas José de San Martín, University of Buenos Aires, Buenos Aires, Argentina.

Objectives: To study the epidemiology of anogenital warts (AGWs) in an Argentinian population of women and the knowledge the women have about these lesions, as well as the emotional impact on their quality of life.

Methods: Prospective observational case-control study including 158 women (mean age 29 years), 98 women with AGWs and 60 without lesions. Sociodemographic data were collected and analyzed. Women with AGWs were surveyed. To measure quality of life in the group of patients with AGWs a self-administered validated questionnaire in Spanish called cuestionario específico para condilomata acuminados (CECA) was used. It is a specific questionnaire for condylomata acuminata (copyright© Dr. Xavier Badia, 2005) that evaluates 10 items and two areas (emotional and sexual areas).

Results: Of 98 patients with AGWs 66% had lesions for the first time; 34% were a recurrent episode. 91% knew the name of the lesion; 77% had detected themselves with the lesion; 18% said it was detected by a doctor and three patients by their partners. 64% knew what warts were; 84% knew they were contagious and 84% knew that there was a treatment for warts. 76% knew about human papilloma virus (HPV). Only 28% used condoms before having warts, while 66% responded they started using condoms after having condylomata acuminata. 47% feared that the lesions would not go away; 77% were worried about having the infection forever; 63% were worried that AGWs would become complicated; 41% felt anxious, depressed, or sad.

Conclusions: Women with AGWs are likely to feel anxious. They fear that the lesions won't go away. Many women know about AGWs however, few used condoms before they developed these lesions.

Recurrent Yeast Infections and Vulvodynia: Can We Believe Associations Based on Self-Reported Data?

BL Harlow^{1,3}, SE Parker¹, D Chatterjee², MP Fox¹, and RHN Nguyen³. ¹Department of Epidemiology, Boston University School of Public Health, Boston MA, USA. ²Macalester College, St. Paul, MN, USA. ³Division of Epidemiology and Community Health, University of Minnesota School of

Public Health, Minneapolis, MN, USA.

Objectives: We determined whether self-reported new or recurrent yeast infections were a risk factor for, and/or consequence of vulvodynia, and then determined the extent to which various levels of misclassification of self-reported yeast infections influenced these results.

Methods: In this case-control study we retrospectively assessed self-reported new and recurrent yeast infections prior and subsequent to first vulvar pain onset among 216 clinically confirmed cases, and during a similar time period for 224 general population controls.

Results: A history of >10 yeast infections prior to vulvodynia onset was strongly, but imprecisely associated with developing the disorder after adjustment for age, age at first intercourse and history of urinary tract infections (aOR=5.5, 95% CI: 1.7–17.8). Likewise, a history of vulvodynia was associated with a 2-fold risk of subsequent new or recurrent onset of yeast infections after adjustment for age, age at first intercourse, and history of yeast infections prior to vulvodynia onset (comparable time period among controls, 95%CI 1.5–2.9). Bias analyses showed that our observed associations were an underestimate of the true association when non-differential misclassification of self-reported yeast infections and certain differential misclassification scenarios were present. However, if women with vulvodynia equally or more accurately self-reported yeast infections when they truly had them compared to controls, but more frequently misreported having them when they truly did not, our observed associations may have been an overestimate of the truth.

Conclusions: To better understand the bi-directional associations between yeast infections and vulvodynia, future validation studies are needed to determine the extent to which misclassification of self-reported yeast infections differ between women with and without vulvodynia.

Survey of ISSVD Membership to Evaluate Areas of Confusion in Pathologist-Clinician Communication

D Heller, MD¹. ¹Rutgers New Jersey Medical School, Newark, NJ.

Objectives: Pathologist-clinician communication has been an ongoing topic in the literature. Pathology reports are geared to assisting clinicians with patient therapy, however at times there are barriers to communication. This survey aims to explore clinicians' understanding of their pathology reports within the membership of the International Society for Vulvovaginal Disease- (ISSVD).

Methods: An email survey was sent to all members of the ISSVD.

Results: Surveys were emailed to 397 members, with 91 responding (23%). Most (76%) of the respondents were gynecologists, with 13% dermatologists and 6% advanced practice nurses. 40% of respondents did not always understand their pathology reports, 62% did not know the difference between levels and recuts, 71% were unclear as to why levels rather than recuts would be ordered, and 26% were not familiar with the term "spongiosis". Over 94% read the gross description on a pathology report. Over 90% reported speaking with their pathologist, which they considered important. They considered having a pathologist with specialty expertise important.

Conclusions: Clinician members of the ISSVD are particularly attuned to the importance of pathology consultation in the care of women with vulvovaginal conditions. There are still areas for potential improvement in educational efforts, particularly providing information on how pathology laboratory processes may impact the report, as well as in further education in dermatopathology terminology.

Care of Male-to-Female Transgender Individuals After Sex Reassignment Surgery: Are Gynecologists/Vulvologists Competent?

C Carriero, PhD¹, M Dellino, MD¹, and G Loverro, PhD¹. ¹Department of Interdisciplinary Medicine, Section Gynecology, University of Bari, Bari, Italy.

Objectives: The gynecologic care of male-to-female (MTF) transgender patients after sex reassignment surgery (SRS) in a setting of vulvar and colposcopy specialists is reported.

Methods: The evaluation of 29 MTF transgender after SRS has been performed at the Center of Colposcopy and Vulvology in the Section of Gynecology of our department. For evaluation of "neovulva" and "neovagina" of MTF transgender females a protocol called LATTEX (Lower Anogenital Tract Transgender Examination) has been created.

Results: For neovulva and neovagina evaluation, the parameters were both aesthetic-anatomical and clinical-functional (sexual). Results of neovulva examination showed that labia minora were well defined only in 10/29 patients, while labia majora were well defined in 22/29, and looked "abnormal" in 7/29

patients. The vaginal introitus was widely permitting in 4/29 and sufficiently permitting in 15/29 patients, while in 10/29 it was even difficult to examine the vagina. In 5/19 patients, the neovagina contained hair and in 7/19 sebaceous secretions. In 7/19 cases the neovagina was eutrophic and elastic. Vaginal sexual activity was referred as absent in 12/29, sporadic in 8/29, and regular with a stable partner in 9/29 cases. Sexual desire, activity, and satisfaction were also evaluated before and after surgery.

Conclusions: Subjects with “sexual dysphoria” (DSM-V) are constantly followed in a multidisciplinary setting, according to World Professional Association for Transgender Health (WPATH) 2011 guidelines. Gynecologists play an important role in caring for transgender patients. In particular, colposcopic and vulvoscopic assessment of neovulva and neovagina, in MTF after SRS, need more standardized criteria, which should be also specific for this special condition.

A Randomized Controlled Trial of Gabapentin in Provoked Vulvodynia: Racial Differences

CS Brown¹, GA Bachmann², C Bachour¹, L Rawlinson¹, J Wan³, and DC Foster⁴.
¹Department of Clinical Pharmacy, University of Tennessee Health Science Center, Memphis, TN, USA. ²Department of Obstetrics, Gynecology and Reproductive Sciences, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ, USA. ³Department of Preventive Medicine, University of Tennessee Health Science Center, Memphis, TN, USA. ⁴Department of Obstetrics and Gynecology, School of Medicine and Dentistry, Rochester, NY, USA.

Supported by a grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Office of Women’s Health Research (HD065740), the University of Tennessee General Clinical Research Center (GCRC) and Depomed, Inc. who provided gabapentin extended release and matching placebo for the study.

Objectives: We compared the efficacy of sustained-released gabapentin compared to placebo in the first multicenter, randomized, double-blind, placebo-controlled trial in women with provoked vulvodynia.

Methods: Eighty-nine participants, 18 years or older, reporting insertional dyspareunia or pain to vulvar touch, fulfilled provoked vulvodynia criteria including localized, vulvar vestibular provoked pain confirmed by cotton swab testing. The primary outcome variable was defined as tampon test pain intensity (numeric rating scale, 0-10) during the last 7 days of the maintenance phase using a randomized, blinded, crossover design with modified intention-to-treat analysis.

Results: Subjects, during the gabapentin crossover phase experienced significantly less pain on the tampon test compared to the placebo phase (mean \pm SE, 3.83 \pm 0.47 vs. 4.28 \pm 0.47, $P = 0.03$), but the difference was not considered clinically significant. When stratified by race, white subjects experienced significantly less tampon test pain during the gabapentin crossover phase (3.41 \pm 0.51 vs. 4.55 \pm 0.52, $P < .01$), whereas black women experienced no significant difference in tampon test pain intensity (5.52 \pm 1.23 vs. 5.62 \pm 1.23, $P = 0.67$). The 1.14 reduction in pain intensity in the primary outcome variable in vulvodynia cases in white women was considered a mild treatment effect.

Conclusions: These data suggest that pharmacologic interventions for pain may be dependent on demographic variables, as white women in this study tended to have a better response, albeit mild response, to gabapentin for vulvodynia pain relief as compared to black women.

Dissecting Vulvodynia Sensory Phenotypes with Intradermal Capsaicin

DC Foster¹, CS Brown², and GA Bachmann³. ¹Department of Obstetrics and Gynecology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA. ²Departments of Clinical Pharmacy, Obstetrics and Gynecology and Psychiatry, University of Tennessee Health Science Center, Memphis, TN, USA. ³Department of Obstetrics, Gynecology and Reproductive Sciences, Rutgers-Robert Wood Johnson Medical Center, New Brunswick, NJ, USA.

Supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Office of Women’s Health Research (HD065740), the University of Tennessee General Clinical Research Center (GCRC) and Depomed, Inc. who provided gabapentin extended release and matching placebo for the study.

Objectives: Sensory phenotype research may provide insight into provoked vulvodynia (PVD) pain chronicity and comorbid associations. We hypothesize

the existence of two PVD sensory phenotypes: with and without measurable post-capsaicin secondary hyperalgesia, an experimental pain index of central sensitization.

Methods: Demographic, medical history, physical exam, and other measures that include intradermal capsaicin testing, were analyzed from the GABA group, an RCT studying gabapentin efficacy for PVD. Post-capsaicin evoked spontaneous pain and secondary hyperalgesia (punctate hyperalgesia and dynamic allodynia) were assessed, among other data points.

Results: Post-capsaicin response segregated into two distinct sensory phenotypes: (0.70) of the cohort with and (0.30) without secondary hyperalgesia. Demographic data and PVD history were indistinguishable by sensory phenotype. Lower genital tract provoked pain and palpable pelvic floor tenderness were also indistinguishable. In contrast, symptoms of overactive bladder, somatic tender point tenderness, measures of depression and anxiety, and screening for sexual abuse were markedly increased in the subgroup displaying capsaicin evoked secondary hyperalgesia. Independent effects on pain threshold/level also were found by racial category but interaction effects between race and sensory phenotypes were minimal. PVD cohort declined further capsaicin experimental pain testing after baseline.

Conclusions: Capsaicin-evoked pain defines two quantifiable PVD sensory phenotypes associated with comorbidity measures and history of sexual abuse. A high discontinuance rate for intradermal capsaicin testing argues for refinement of alternative methods for future research.

Environmental Exposures and Risk of Vulvodynia: Unrecognized Risk Factors

BD Reed, MD, MSPH¹, KS McKee, PhD, MPH¹, MA Plegue, MS¹, HK Haefner, MD², SK Park, ScD, MPH³, and SD Harlow, PhD³. ¹Department of Family Medicine, University of Michigan Health Systems, Ann Arbor, MI, USA. ²Department of Obstetrics and Gynecology, University of Michigan Health Systems, Ann Arbor, MI, USA. ³Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, MI, USA.

Objectives: Vulvodynia is a chronic pain condition associated with sensitivity of the vulva, but risk factors are poorly understood. Due to the potential impact of environmental exposures on neurotoxicity and immunoreactivity, we assessed the association between past environmental exposures and risk of vulvodynia.

Methods: Recalled exposures to 28 past environmental chemicals at home or work were queried at the 24-month survey in the longitudinal population-based Woman-to-Woman Health Study. Vulvodynia case status was defined on biannual surveys from baseline through 24 months as 1) meeting case criteria, or 2) having intermediate symptoms, and each was compared to those never having had vulvodynia symptoms. Multinomial regression models were used to evaluate the relationship between vulvodynia status and environmental exposures (assessed individually and aggregated into 8 categories), with and without adjustment for age, ethnicity, and socio-economic status.

Results: Data on 1,585 women met criteria for inclusion (325 vulvodynia cases, 301 with intermediate symptoms, and 959 controls). Eleven of the 28 individual exposures were increased in vulvodynia cases ($p < 0.05$ after adjustment), with increased risk associated with the following categories: occupational exposure to solvents or paints (OR=2.1; 95% CI=1.3-3.4), reporting exposures to chemicals used in or around the home (OR= 1.9; 95%CI=1.3-2.8), employment as a housekeeper (OR=1.8; 95%CI=1.2-2.6), and use of rodent poison or mothballs at home (OR=1.4; 95%CI=1.1-1.9).

Conclusions: Past environmental exposures were associated with current/recent vulvodynia. Future research is needed to confirm these findings, to identify specific chemical agents, dose and timing of exposure, and to identify factors associated with increased susceptibility to these toxins.

Systematic Review of Treatment Outcomes for Vulvodynia

LA Sadownik, MD^{1,2}, P Yong, MD², A Syed³, and KB Smith, PhD¹². ¹BC Centre for Vulvar Health, University of British Columbia, Vancouver, BC, Canada. ²Department of Obstetrics and Gynecology, University of British Columbia, Vancouver, BC, Canada. ³University of Manchester, Manchester, UK.

Objectives: Systematically evaluate the literature regarding treatment outcomes for vulvodynia. Identify reported outcomes of vulvodynia treatments and categorize these into 3 core domains: (1) pain; (2) physical/sexual functioning and (3) emotional functioning.

Methods: Databases (MEDLINE via OVID, PubMed, and PsycINFO) were searched using MeSH terms related to vulvodynia/treatment. Studies were included if: English full text; original research published in a peer-review journal; objective of study or first reported outcome was to evaluate the outcome of a vulvodynia treatment; study population included only women >18 years of age with vulvodynia; and the study design was a randomized trial or a well-designed prospective observational case series. Three authors independently sorted all studies. Selected studies were then analyzed.

Results: There were 206 articles identified for full-text screening, 33 of which met the criteria. The most commonly reported outcome was "pain with intercourse" with 25/33 of studies reporting explicitly about this outcome. The most common standardized instrument used to elicit this outcome and general sexual function was the Female Sexual Function Index (13/33). There was a broad range of investigator-derived questions regarding sexual intercourse that varied in format, content and scales used. The McGill Pain Questionnaire was used in 14/33 studies. Clinical outcomes included: pain with Q-tip exam (11/33), pain threshold of vestibule (7/33), and pain with gynecologic exam (5/33). There was a lack of standardization of the method to obtain and report these outcomes. The most common tool used to report emotional outcomes was the Beck's Depression Index (6/33).

Conclusions: A core set of standard vulvodynia treatment outcomes would support the meta-analysis of research in the field.

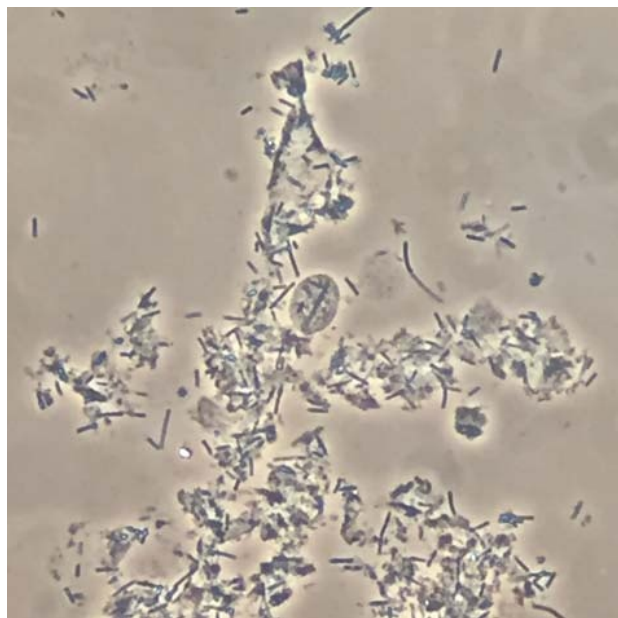
Vaginal Flora Influences the Risk of Vulvodynia

P Vieira-Baptista, MD¹, J Lima-Silva, MD¹, J Xavier, MD¹, J Beires, PhD¹, and G Donders^{2,3,4}. ¹Department of Obstetrics and Gynecology, Centro Hospitalar de São João, Porto, Portugal. ²Femicare vzw, Clinical Research for Women, Tienen, Belgium. ³Department of Obstetrics and Gynecology, University Hospital Antwerpen, Belgium. ⁴Department of Obstetrics and Gynecology, General Hospital H Hart, Tienen, Belgium.

Objectives: The cause(s) of vulvodynia remain largely unresolved. We have postulated that vaginal flora, with inherently different interleukin and pH profiles can play a role in the development or severity of the condition.

Methods: Vaginal slides from vulvodynia patients (97) were compared with an historical control group (women referred for abnormal Pap test or for family planning services). Cases for the control group were randomly age-matched at a ratio 2:1 with the study group. Slides were graded according to Femicare's criteria¹. Women in the study group were only considered a case if symptoms (burning/pain) persisted after correction of the first situation.

Results: The presence of bacterial vaginosis and Candida were associated with a lower risk of vulvodynia. On the contrary, cytolytic vaginosis (CyV) (Image 1) was strongly associated with vulvodynia as compared to normal controls (OR 4.6 (CL95 1.89-11.16)). See image 2



	Vulvodynia (97)	Control (194)	OR (CL95)	P value
msAV	10.3%	8.8%	1.197 (0.526-2.723)	0.668
AV (any)	21.6%	20.1%	1.098 (0.604-1.996)	0.759
BV	1.0%	14.9%	0.059 (0.008-0.442)	0.000
AVF (LB grade IIb+ III+absent)	33.0%	42.8%	0.658 (0.395-1.096)	0.107
Candida	23.7%	35.6%	0.563 (0.324-0.978)	0.040
Cytolytic vaginosis	16.5%	4.1%	4.593 (1.890-11.160)	0.000

msAV - moderate or severe aerobic vaginitis; AV - aerobic vaginitis; BV - bacterial vaginosis; AVF - abnormal vaginal flora; LB - lactobacilli

Conclusions: Vaginal flora can affect vulvodynia. This can be due to chronic exposure of the vestibule to very low pH, hydrogen peroxide and acids. The lower risk associated with Candida could be due to a bias as these women are more likely over treated with antifungals. We advise providers to search for CyV in vulvodynia patients and attempt correction if possible, before engaging in more intensive therapies. Also, as moderate/severe Aerobic Vaginitis can be linked to severity of vulvodynia, and CyV to its frequency, wet mount microscopy is fundamental in women with vulvar pain or burning.

Manual Techniques Aimed at Easing Chronic Vulvar Pain Prior to Internal Assessment

D Hartmann¹ ¹Dee Hartmann Physical Therapy, Chicago, IL, USA.

Objectives: Reducing abnormal tension in pelvic floor muscles (PFMs) in women with vestibulodynia (provoked vestibulodynia or PVD) was found by Glazer et al. in 1995 to improve sexual function and decrease complaints of chronic vulvar pain. Multiple studies since have confirmed the presence of abnormal tension in PFMs in women with PVD when compared to matched, asymptomatic controls. Though its pathophysiology remains unclear, PVD may be caused by inciting events in patients' histories. Histories that include recurrent yeast or bacterial infections, urinary or bladder infections, endometriosis, or chronic bowel dysfunction can have a lasting, negative impact, causing PFM dysfunction as well as elevated tension in the affected viscera. Though this may not occur in all, many women with PVD present with both elevated PFM tone and residual abnormal visceral tension. Though PFM dysfunction appears to be a primary driver of chronic vulvar pain, it is possible that the muscular dysfunction is secondary to abnormal tension in the surrounding abdominal and pelvic viscera, fascia, and muscle. Together, these abnormal physical findings make internal assessment, whether digital or with a speculum, painful, difficult at best, or often impossible.

Methods: The faces and verbal responses of 5 women with chronic vulvar pain were recorded by a professional cinematographer prior to, and following instruction in and completion of, 5 patient-performed activities. The activities, meant to decrease tension in abdominal and pelvic viscera, fascia, and muscles, included 1) deep, lateral, diaphragmatic breathing; 2) stretching the urachus on the lower abdominal wall; 3) stretching the deep hip muscles; 4) bridging; and 5) actively contracting and relaxing the PFMs. Changes in subjective vulvar pain were measured using digital palpation at 3, 6, and 9 o'clock on the vulva using the perceived pain index (PPI) of 0-10/10 pain.

Results: All 5 women responded favorably to the simple techniques, reporting immediate increased comfort, decreased palpated vulvar pain, and reduced anxiety. All palpated PPI scores decreased by more than 3 points on the 0-10 scale.

Conclusions: When working with women with PVD using the described techniques, healthcare providers—physicians, nursing professionals, physical therapists—can begin to assure women and to give them hope, while still in the clinic, that their vulvar pain may be manageable from a functional, physical perspective. The techniques introduced are easily transferable to any clinic setting, providing medical practitioners with strategies to immediately decrease tissue tension, reduce anxiety, and lessen palpated vulvar pain prior to performing digital or speculum vaginal exams.

A Much-Needed Model for the Preclinical Testing of New Vulvodynia Therapies

ML Falsetta¹, DC Foster², AD Bonham², MA Linder², SJ Pollock¹, CG Haidaris³, and RP Phipps^{1,2,3}. ¹Department of Environmental Medicine, University of Rochester, Rochester, NY, USA. ²Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY, USA. ³Department of Microbiology and Immunology, University of Rochester, Rochester, NY, USA.

Objectives: There is no single effective treatment for localized provoked vulvodynia (LPV), the most common cause of dyspareunia. Following our in vitro work that established a link between inflammation and LPV pain, we developed a preclinical model to test new/promising LPV therapeutics and monitor pain/inflammation in vivo.

Methods: We improved an existing mouse model of LPV to assess therapeutic intervention against vulvar pain; we incorporated and validated new techniques (e.g. video monitoring of mouse behavior, the use of an electronic von Frey system for pain testing, weight assessment, and proinflammatory mediator quantification) to facilitate thorough and objective monitoring of pain and inflammation over time.

Results: We established stable allodynia (lasting months) in three mouse strains (one outbred, two inbred); reproducible pain thresholds values were generated using an electronic vonFrey system. During allodynia induction, we found that pain thresholds decreased with weekly subdermal vulvar injections of zymosan (yeast cell wall product), while mice receiving placebo (saline) failed to develop or only developed transient allodynia. In conjunction with reduced pain thresholds, we observed an increase in proinflammatory mediator levels (e.g. prostaglandin E2) within collected vulvovaginal fluids, consistent with previous in vitro findings. After establishing allodynia, we treated with pro-resolving agents that mitigate zymosan-associated inflammation; preliminary results suggest treatment can restore pain thresholds to pre-induction levels.

Conclusions: We have made a significant advance in vulvar pain research through the development of a mouse model to monitor pain and inflammation (in real time), which will facilitate the necessary preclinical testing of new vulvodynia therapies.

Vulvar Cancer: Epidemiology and Treatment in Different Countries

L Micheletti, MD¹, M Preti, MD¹, and G Radici, MD¹. ¹Department of Gynecology and Obstetrics of the University of Torino, S. Anna Hospital, Torino, Italy.

Vulvar cancer is a rare malignancy with an incidence ranging from 1.6 to 2.4 per 100,000 women. In some countries, an increase in overall incidence rate has been reported: in Germany, the incidence rate has doubled from 1.7 to 3.6 from 1999 to 2011, in Denmark a 1.97% increase in incidence rate per year from 1978 to 2007 has been reported, similarly in USA between 1973 and 2000 a 1.0% per year increase in incidence has been noted. In Australia from 1982 to 2009 a far less increase, from 2.1 to 2.5 per 100,000 women, has been observed.

Surgery still represents the standard treatment for any primary lesion confined to the vulva. However, by the end of the 1980s, the Taussig and Way en block vulvectomy with bilateral groin dissection has been gradually replaced by the 'conservative and individualized approach'. Safe surgical conservative modifications, today unanimously accepted, are: separate skin vulvar-groin incisions, wide local radical excision or partial radical vulvectomy in the case of tumor less than 3-4 cm, omission of groin lymphadenectomy only when the tumor stromal invasion is ≤ 1 mm, unilateral groin lymphadenectomy only in well-lateralized early lesion, and total groin lymphadenectomy with preservation of femoral fascia when full groin resection is needed. Sentinel lymph node biopsy is a reliable method, but should not be routinely employed outside referral centers.

Adjuvant radiation is indicated in presence of groin lymph node metastasis.

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Uncommon Vulvar Lesions

M Sluga, MD¹. ¹Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Objectives: To show uncommon cases of vulvovaginal disease.

Methods: We selected 6 cases of uncommon vulvar diseases seen at the Vulvar Pathology section of the Hospital Italiano of Buenos Aires where the disease diagnosis has been a challenge.

Results: Case 1. Vulvar fixed drug eruption in an 82-year-old woman related to analgesic intramuscular injection. The diagnosis was made by exclusion after ruling out other causes for the vulvar ulcers. The skin lesions resolved immediately when the offending drug was ceased. Case 2. Vulvar pemphigus vegetans (Hallopeau type) in a 56 y.o. patient. The diagnosis was made by clinical presentation, direct immunofluorescence, and histopathology demonstrating hyper eosinophilia. Treatment consists of systemic steroids and azathioprine. Case 3. Glomus tumor in a 26 y.o. patient who was evaluated for a painful tumor on the clitoris. The tumor was initially misdiagnosed as an epidermal inclusion cyst. The correct diagnosis was made by histopathology after complete excision of the tumor Case 4. Chondroid syringoma in a 78 y.o. patient. The diagnosis was made by histopathology after removing the entire lesion. Case 5. Ectopic mammary gland tissue in the vulva of a puerperal patient. The diagnosis was made by the clinical presentation, puncture aspiration of a vulvar cyst, and confirmed by histopathology. The treatment consisted of lactation suppression and excision of the remaining cysts. Case 6. Chronic lymphocytic leukemia presenting as vulvar ulcers in a 67 y.o. patient with a history of non B cell Hodgkin lymphoma. Symptomatic treatment was applied locally and systemic management of the leukemia was initiated.

Conclusions: Regardless of their low frequency, we should take these uncommon pathologies into account for differential diagnoses.

Short and Long-Term Efficacy of Focused Ultrasound Therapy for Lichen Simplex Chronicus, Lichen Sclerosus, and Lichen Planus

C Li¹. ¹The College of Biomedical Engineering, Chongqing Medical University, Chongqing, China.

Objectives: To investigate the short and long-term efficacy and influential factors of focused ultrasound for the treatment of lichen simplex chronicus, lichen sclerosus, and lichen planus.

Methods: A total of 136 eligible patients with lichen sclerosus and lichen planus were included in this study and treated with focused ultrasound. According to the terminology of the International Society for the Study of Vulvovaginal Disease (ISSVD), 85 of the patients with vulvar disease had lichen simplex chronicus (LSC), 44 patients had lichen sclerosus (VLS), and 7 patients had lichen planus (LP). Patients were followed up regularly after treatment. The efficacy of ultrasound therapy was evaluated based on degrees of itching, physical signs and pathological changes in lesions. The relations between age, course, menopause status, pathological type and improvement with treatment were analyzed. Statistical analysis was performed using the χ^2 (McNemar χ^2) test.

Results: The average follow-up period was 23.8 months (range 3 months to 60 months). 68 of 136 patients fully recovered (cure rate 50%). 59/136 (43.4%) were found to have some improvement resulting in an efficacy of 93.4% (127/136). 6.6% (9/136) found the treatment to be ineffective. 7/127 (5.51%) of the patients with improvement recurred. No severe side effects were found during treatment and no complications were observed during follow-up. The age, course of disease, and status of menopause were related to the efficacy ($c^2=21.017$, $P=0.000$; $c^2=26.591$, $P=0.000$; $c^2=8.199$, $P=0.000$). There was no significant difference in the efficacy of different pathological types ($c^2=1.635$, $P=0.442$).

Conclusions: Focused ultrasound is safe and effective for lichen simplex chronicus, lichen sclerosus, and lichen planus. The efficacy is correlated with age, menopause status, and course.

Cytolytic Vaginosis Does Not Have an Impact on Human Papilloma Virus (HPV) Infection and Cervical Dysplasia

P Vieira-Baptista, MD¹, J Lima-Silva, MD¹, S Tavares, MD¹, J Beires, PhD¹, and G Donders^{2,3,4}. ¹Department of Obstetrics and Gynecology, Centro Hospitalar de São João, Porto, Portugal. ²Femicare vzw, Clinical Research for Women, Tienen, Belgium. ³Department of Obstetrics and Gynecology, University Hospital Antwerpen, Belgium. ⁴Department of Obstetrics and Gynecology, General Hospital H Hart, Tienen, Belgium.

Objectives: Cytolytic vaginosis (CyV) is characterized by an increased number of lactobacilli in the vagina and epithelial cell lysis, most likely due to an excessively low pH. In this study, we examined the hypothesis of the existence of a relation between the premature and increased rupture of epitheliocytes and the risk of cervical dysplasia and HPV infection.

Methods: Consecutive women referred for consultation due to an abnormal Pap test or for family planning services were evaluated using wet mount microscopy, Pap test, HR-HPV test (cobas®, Roche), and biopsy of the transition zone according to current national guidelines.

Results: The prevalence of CyV among the 1,022 evaluated women was 3.1%. There were no differences in the prevalence between women with a normal and an abnormal Pap test (3.5% vs. 2.6%, $p=0.4$) nor between those with a normal Pap test or with minor abnormalities (ASC-US/LSIL) and more concerning abnormalities (3.2% vs. 2.8%, $p=0.8$). There were also no differences in the prevalence of CyV in women who were HR-HPV positive vs. those who were negative (2.7% vs. 3.5%, $p=0.5$); nor in those with or without HPV 16 (3.0% vs. 3.8%, $p=0.6$) or HPV 18 (3.0% vs. 5.7%, $p=0.4$). Amongst women who had a cervical biopsy ($n=321$), CyV was slightly more frequent in high-grade lesions than if histology was CIN1 or less (4.2% vs. 1.8%), but the difference was not statistically significant ($p=0.3$).

Conclusions: CyV is found in 3.1% in a random population. Opposed to the previously reported association with aerobic vaginitis, our data do not support a relation between CyV and HR-HPV infections or cervical dysplasia.

Multidisciplinary Management of Extramedullary Multiple Myeloma of The Vulva: A Case Report

SM Fragomeni, MD¹, G Garganese, MD¹, and G Scambia Professor¹. ¹Department of Gynecologic Oncology, Catholic University of the Sacred Heart of Rome, Italy.

Objectives: Extramedullary plasmocytoma (EMP) is an uncommon condition. It rarely occurs on the vulva, with less than 10 cases described in literature.

Methods: A retrospective case report of a patient with a clitoral extramedullary plasmocytoma is presented.

Results: A 39-year-old woman with history of micromolecular multiple myeloma (diagnosed in 2014 and treated with systemic chemotherapy and autograph), was diagnosed in 2015 with an extramedullary relapse in two different sites 1) muscles of the left leg and 2) vulva. The patient was referred to our institution and the clinical examination showed a 2-cm mobile mostly exophytic nodule with a rounded, elastic, smooth surface which involved the lower third of the anterior/right vestibule (fig.1). Evaluation was completed including: i) groin ultrasound, negative for lymphadenopathy ii) pelvic MRI, negative for ureteral infiltration iii) 11C-Methionine PET/CT scan, positive for focal radiotracer uptake and iv) vulvar biopsy, positive for EMP. After multidisciplinary evaluation (gynecologic oncology surgeon, radiation oncologist and hematologist-oncologist) systemic chemotherapy was provided. After completion of the regimen, clinical/instrumental assessments showed a complete muscular response and a stable vulvar lesion. Vulvar surgery was considered feasible. The patient underwent an antero-lateral partial vulvectomy (fig.2). The pathological report confirmed an EMP with negative resection margins. Radiation was not indicated. Function was preserved and the patient was referred for regular follow up. Clinical visits at 3, 6, 9 and 12 months were negative for local-regional recurrence.

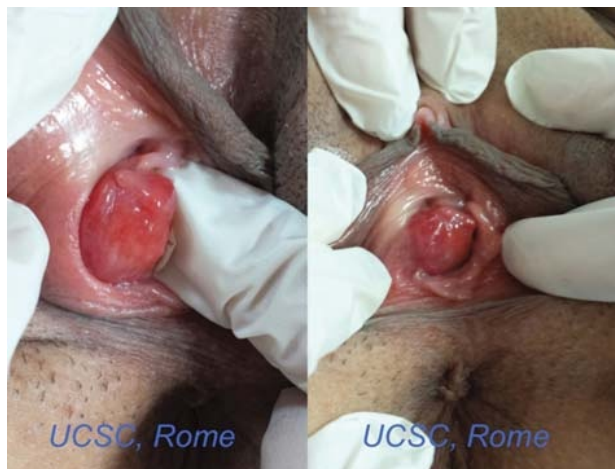


FIGURE 1. Clinical presentation.



FIGURE 2. Vulvar resection.

Conclusions: The use of a multidisciplinary approach including a combination of chemotherapy and surgery resulted in adequate local and systemic control.

Vulvodynia: Item Development of a Self-Report Outcome Measure for Quality of Pain

CS Brown¹, M Goetsch², GA Bachmann³, K Smith⁴, S McDonough¹, and C Pukall⁵. ¹Department of Clinical Pharmacy, University of Tennessee Health Science Center, Memphis, TN, USA. ²Department of Obstetrics and Gynecology, Oregon Health and Science University School of Medicine, Portland, OR, USA. ³Department of Obstetrics, Gynecology and Reproductive Sciences, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ, USA. ⁴Department of Obstetrics & Gynaecology, University of British Columbia, Canada. ⁵Department of Psychology, Queen's University, Kingston ON, Canada.

Objectives: The National Institutes of Health initiated the Patient-Reported Outcomes Measurement Information System (PROMIS®) network for uniformly assessing pain in research and patient care; however, a specific outcome measure for vulvodynia pain has not been developed to date. We describe item development of a self-report outcome measure for quality of vulvar pain in women with vulvodynia using the PROMIS® process for item selection.

Methods: The PROMIS® process for item selection includes conduction of a systematic literature review, item classification and selection, item review and revision, focus group input on domain coverage, cognitive interviews with individual items, and final revision before field-testing.

Results: 140 items were identified from widely accepted legacy measures in the literature, including the PROMIS® generic pain measures, McGill Pain Questionnaire, Brief Pain Inventory, and Vulvodynia Pain Assessment Questionnaire. Of those 140 items, a vulvodynia working group identified 51 items and four domains relevant to this condition, including burning pain, incisive pain, sensitivity pain, and emotional response. Five centers will conduct 1) two focus groups of six vulvodynia patients to confirm domain definitions and to add additional items and 2) four cognitive interviews to identify problematic items. Construct and discriminant validity will also be tested.

Conclusions: This measure will capture women's experiences of the quality of vulvar pain in a structured format, and add to the overall understanding of symptoms from affected women's perspectives. This work will advance patient-centered outcomes research and clinical care and guide future development of vulvodynia symptom measures.

The Utility of the Lidocaine Test in the Diagnosis of Localized Provoked Vulvodynia

A Stenson, MD, MPH¹, C Leclair, MD¹, and M Goetsch, MD¹. ¹Program in Vulvar Health, Department of Obstetrics and Gynecology, Oregon Health & Science University.

Objectives: The purpose of this study was to evaluate the lidocaine test as a means of clarifying the mucosal locus of pain in localized provoked vulvodynia (LPV).

Methods: Reproductive-age patients presenting with dyspareunia and clinical history consistent with LPV were recruited to participate in a prospective cohort study. Demographics and clinical data were recorded. Each participant had a standard cotton swab test (CST) of the vulvar vestibule at 6 points. Participants reported pain using a numeric rating scale 0-10 (NRS). Lidocaine 4% topical solution was then applied to the vestibule for three minutes and the CST repeated. Change in NRS at each point was analyzed by paired t-test.

Results: 16 patients completed the study. Mean age was 28.0 (+/- 4.6) years. Half of the participants (50%; n=8) had primary LPV and the rest had secondary. Participants reported symptoms for an average of 5.8 (+/-4.5) years. A history of abuse was reported by 25%. The majority (n=14) were nulligravid. All examinations were negative for vulvovaginitis and dermatoses. Participants reported highest pain at 4-8 o'clock. Lidocaine significantly reduced pain scores at all 6 points (see table 1.)

Conclusions: Lidocaine significantly reduced vestibular allodynia in paired cotton swab testing in participants with LPV. The finding that lidocaine extinguishes vestibular pain supports the theory that LPV is a superficial neuroproliferative condition of the mucosa. A successful lidocaine test can strengthen the diagnosis of LPV. This is the first detailed explication of this technique in premenopausal women with LPV.



Vulvar Myoepithelial Tumor

SCAV Fialho, PhD¹, DAS Monteiro², ICCV Guimarães, PhD¹, BO Vasconcellos², JL Xavier², JAS Pantaleão, PhD¹, and L Pantaleão³. ¹Department of Maternal and Child Health, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ²Residents in Obstetrics and Gynecology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ³Department of Pathological Anatomy, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil.

Objectives: A case report of a vulvar myoepithelial tumor.

Methods: Retrospective case report.

Results: A 20-year-old was referred to Antonio Pedro University Hospital (HUAP) with a 3-month history of an enlarging vulvar mass and severe pain. She reported continued/worsening of her symptoms despite antibiotic therapy. An ultrasound 2 months prior to her visit contained a 40.6 x 34.3 mm subcutaneous tumor in the left perineal region. Physical examination confirmed a solid and mobile tumor with inflammatory changes involving the left labium majus, perineum, and inguinal region. There was a central ulcerated area likely secondary to friction. A biopsy was nonspecific with chronic inflammatory changes and lymphedema. Magnetic resonance imaging confirmed a superficial, heterogeneous lesion. Excision was performed with histopathology demonstrating a myoepithelial



soft tissue tumor with moderate pleomorphism, suggestive of a myoepithelial carcinoma. The patient was referred to oncology for continued care.

Conclusions: Myoepithelial carcinoma, defined in 1975, is a malignant tumor arising mainly from the parotid gland. Myoepithelial carcinoma of soft tissue is rare compared to its salivary gland homologue and shows a more aggressive behavior with recurrence and metastasis in up to 40-50% of the cases. Given the rarity of this disease and its uncertain prognosis, there are no clinical trials regarding the need for adjuvant therapy. Early diagnosis is essential to optimize treatment and outcome.



Atypical Manifestations of Genital Herpes in Immunosuppressed Patients

SCAV Fialho, PhD^{1,2}, ICCV Guimarães, PhD¹, DAS Monteiro³, BO Vasconcellos³, JL Xavier³, and M Rochael¹. ¹Department of Maternal and Child Health, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ²Candidate for Fellowship, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil. ³Residents in Obstetrics and Gynecology, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil.



⁴Department of Pathological Anatomy, Hospital Universitário Antônio Pedro, Universidade Federal Fluminense, Niterói, RJ, Brazil.

Objectives: To report 3 cases of immunosuppressed patients with atypical manifestation of genital herpes (HSV) treated at the ambulatory of Vulvar Pathology of the University Hospital Antônio Pedro.

Methods: Retrospective review including 3 immunosuppressed patients with genital herpes treated at a single institution.

Results: Case 1: an 82 year old, with chronic lymphocytic leukemia, referred for evaluation of a vulvar lesion. Upon examination woody edema and painless ulcers with reddish edges and yellowish background, suggestive of fibrin were noted involving the left labium. Additionally a mobile inguinal lymph node was identified on the right. Case 2: a 37 year old, HIV positive patient, referred for evaluation of a vulvar lesion. Upon examination an approximately 8 cm painless, red, soft vegetative lesion with well delimited edges and serous secretion was noted. Additionally mobile and enlarged painful right inguinal lymph node adenopathy was present. Case 3: a 62 year old, with extensive ulcerated lesions on the vulva with purulent secretions and a fetid odor; bilaterally painful inguinal lymph nodes. In each case histopathology confirmed infection caused by herpes virus. In all three cases immunohistochemistry was positive for HSV-1 and HSV-2. All were treated with intravenous acyclovir. One case required intravenous foscarnet for acyclovir resistance.

Conclusions: The herpes simplex virus is the most common cause of genital ulcers in the world, being responsible 40% of the cases in Brazil. Immunosuppression influences the incidence, severity, and presentation of various opportunistic diseases. Resistance is caused by mutations in the viral thymidine kinase or DNA polymerase gene. Most cases of antiviral resistance are susceptible to other drugs that do not require the activation of thymidine kinase, such as foscarnet.

Profiling a Cohort of Vulvodynia Patients

S Johns¹, M Jantos², and E Baszak-Radomańska³. ¹BNurs, MMid, School of Nursing and Midwifery, University of South Australia. ²Behavioural Medicine Institute of Australia & Department of Human Anatomy, Medical University of Lublin, Poland. ³Terpa Clinic, Lublin Poland.

Objectives: To identify characteristics of a vulvodynia cohort, including, age related prevalence, comorbidities, description of pain, sexual history, and to determine differences between women of reproductive age (RA) and post-reproductive age (PRA) in relation to gynecological, urological and gastroenterological symptoms reported.

Methods: This is a retrospective study based on a database of 1143 women diagnosed with vulvodynia. The age ranged between 18-70 years. The study was approved by the University of South Australia's Human Research Ethics Committee.

Results: Vulvodynia prevalence peaked at age 25, with 76.6% of cohort under the age of 35 years. By age 36, prevalence decreased noticeably and plateaued from age 37 onwards as seen in Figure A. A comparison of gynecological, urological and gastroenterological symptoms between RA and PRA women showed a notable increase in incidence of cysts, dysuria, bladder pain syndrome (BPS)/interstitial cystitis, frequency, incontinence and gastro-intestinal

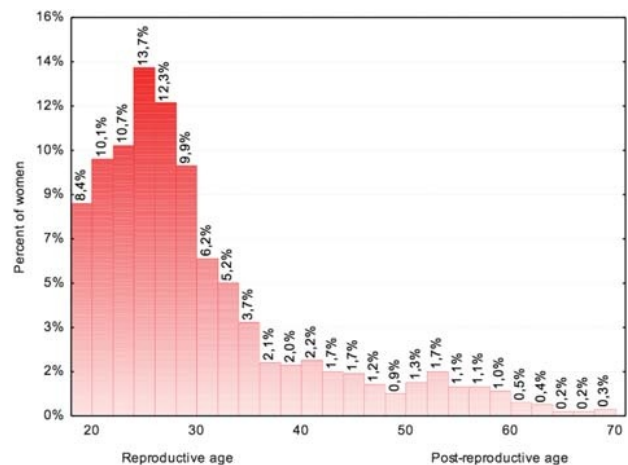


FIGURE A. Age related prevalence

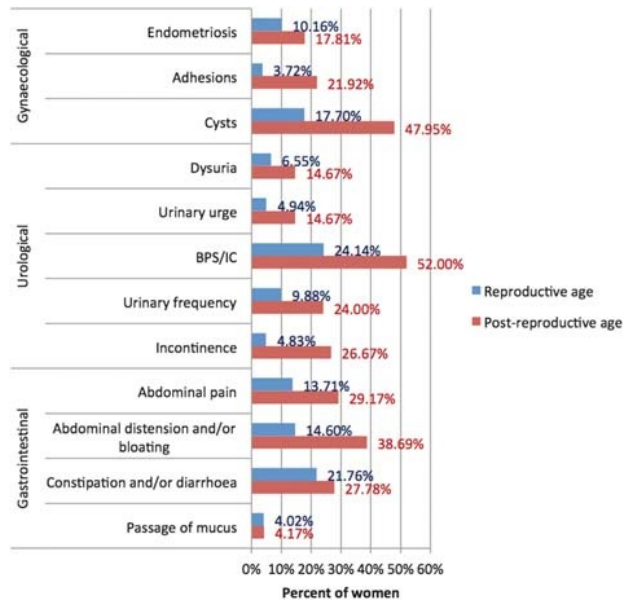


FIGURE B. Comparison of symptoms between reproductive and post-reproductive age women.

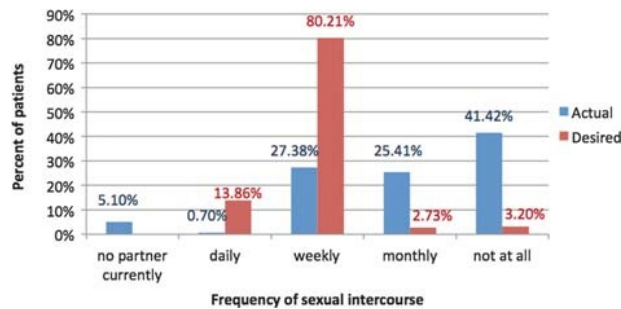


FIGURE C. Comparison of mean pain scores for Vd, BPS and controls

symptoms as shown in Figure B. Analysis of data showed the significant impact that vulvodynia has on quality of life and limitations it imposes on sexual activity as reflected in Figure C. Almost half of women with chronic urethral pain (CUP) were sexually abstinent (41.4%).

Conclusions: This study identifies age related prevalence, symptoms and changes in sexual function that impact vulvodynia sufferers. The findings provide insight into this complex pain syndrome.

Figure C: Difference between actual and desired frequency of intercourse.

Testing the Reliability of Q-tip Criteria in the Diagnosis of Vulvodynia

M Jantos¹, S Johns², and E Baszak-Radomańska, MD, PhD³. ¹Behavioural Medicine Institute of Australia & Department of Human Anatomy, Medical University of Lublin, Poland. ²BNurs, MMid, School of Nursing and Midwifery, University of South Australia. ³Terpa Clinic, Lublin Poland.

Objectives: This study sought to establish the validity of the Q-tip test in the diagnosis of vulvodynia by comparing pain scores from multiple points in the vulvar, pelvic and paraurethral region and comparing them with vulvodynia, asymptomatic controls and general gynecology sample without pain.

Methods: A total of 320 pain maps were analyzed from 238 women with a diagnosis of vulvodynia [119 vulvodynia only, 119 vulvodynia + bladder pain syndrome (BPS)], 29 BPS, 32 asymptomatic controls and 21 general gynecology cases not presenting with pain. A total of 52 points were palpated. The study was approved by the University of South Australia’s Human Research Ethics Committee.

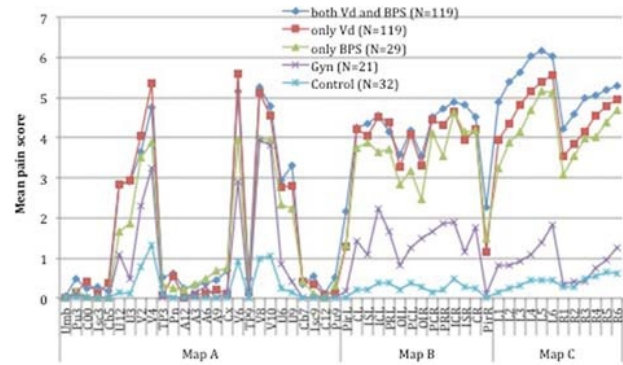


FIGURE 1. Comparison of mean pain scores for Vd, BPS and controls

Results: All groups were comparable in terms of age and parity. Pain scores were considered clinically significant if they were ≥ 2 . A summary of pain scores for all groups is shown in Graph A. In vulvodynia women, the highest scores were recorded in the paraurethral area. The pain scores of the gynecology cases closely approximated those of vulvodynia women. Women in the control group reported pain on all vestibular points (V 2, 4, 6, 8, 10), but were significantly lower than the vestibular pain scores of vulvodynia and general gynecology cases. Regression analysis showed that for a reliable diagnosis of vulvodynia the following points need to be examined; vestibule (V6), urethra (U9), pelvic ischial left (ISL) and puborectalis right (PRR), and two left paraurethral points (CL2 and CL5). Graph A. Pain mapping score comparisons for vulvodynia, vulvodynia + BPS, BPS, Gynecology group and Controls.

Conclusions: Past and present diagnostic criteria focus primarily on the mapping of pain in the vulvar vestibule and the inner thighs. Given that asymptomatic women also show hypersensitivity in the vestibule and that general gynecology cases present with significant pain in the vestibule, other points identified in this study must be added for a reliable diagnosis of vulvodynia as reliance of the Q-tip test in the vestibule is not reliable in differentiating between vulvodynia and non-vulvodynia cases.

Vulvodynia and the Validity of its Sub-Classifications: Evidence from Pain Mapping

M Jantos¹, S Johns², and E Baszak-Radomańska³. ¹Behavioural Medicine Institute of Australia, South Australia & Department of Human Anatomy, Medical University of Lublin, Poland. ²BNurs, MMid, School of Nursing and Midwifery, University of South Australia. ³Terpa Clinic, Lublin Poland.

Objectives: Using pain mapping, this study seeks to examine the validity of the ISSVD sub-classification of vulvodynia as provoked, spontaneous and mixed.

Methods: A total of 238 women diagnosed with vulvodynia met the inclusion criteria, and were subdivided into provoked (VdP) (n=115), spontaneous (VdS) (n=111), and mixed (VdM) (n=12). Comparison of pain mapping scores with asymptomatic controls (n= 32) and general gynecology patients (n=21) was performed. A total of 52 points were assessed. The study was approved by the University of South Australia’s Human Research Ethics Committee.

Results: Significant differences in pain scores between vulvodynia and control groups existed for 36/52 palpation points. When comparing VdP and VdS only two points, which have no diagnostic value, showed significant differences. Vulvodynia subgroups and controls were comparable in terms of age and parity. Graph 1: Comparison of mean pain scores for vulvodynia subgroups and controls

Conclusions: Pain mapping reliably differentiated between vulvodynia and asymptomatic controls. However, the sub-classification of VdP and VdS cannot be distinguished on the basis of pain mapping scores. Functionally, both VdP and VdS cases can identify specific triggers of pain during physical examination and intercourse, but the pain mapping profile of these subgroups is the same. While sub-classification is traditionally based on reported symptoms, pain mapping is based on physical examination. The lack of difference in pain scores between vulvodynia sub-groups makes the distinction between the two groups appear artificial and irrelevant.

Female Genital Mutilation as a Cause of Inclusion Cysts

A Amin¹ and S Mekki². ¹Elobeid Obstetrics & Gynecology Teaching Hospital, North Kordofan, Sudan. ²University of Kordofan, Kordofan, Sudan.

Objectives: To review a patient with a vulvar inclusion cyst in the setting of female genital mutilation.

Methods: Results: A 78-year-old multiparous and menopausal woman was brought by her daughter to emergency department, after she noticed that there was a restriction in her physical movement as well as abnormal walking. On examination, patient looked well, not in pain and all vital signs were within the normal ranges. The abdominal examination showed neither masses nor tenderness. Genital examination revealed a huge vulvar inclusion cyst (as demonstrated in the photo) measuring 13x13cm. There were no ulcers or erosions. Surgical excision was performed under spinal anesthesia with transverse rounded incision with confirmation of a vulvar inclusion cyst in the setting of female genital mutilation (FGM).

Conclusions: It is important to consider the multidisciplinary cultural and social complexity of traditional Sudanese community when addressing FGM. Efforts to fight FGM are, and have always been, criticized by conservative community and religious leaders who advocate for Sunna circumcision (excision of prepuce and the clitoris) as part of religion demands. The United Nations



FIGURE 1. A patient with a vulvar inclusion cyst in the setting of female genital mutilation.

Children's Fund (UNICEF) Multiple Indicator Cluster Surveys report of 2014 demonstrated that the 86.6% of women in Sudan from the age group (15 – 49) have undergone a FGM, while 31.5% of girls from the age group (0-14) were victims of FGM.