



## Vulvodynia: Assessment and Treatment

Andrew T. Goldstein, MD,<sup>1\*</sup> Caroline F. Pukall, PhD,<sup>2\*</sup> Candace Brown, PharmD,<sup>3</sup> Sophie Bergeron, PhD,<sup>4</sup> Amy Stein, DPT,<sup>5</sup> and Susan Kellogg-Spadt, PhD<sup>6</sup>

### ABSTRACT

**Introduction:** Vulvodynia constitutes a highly prevalent form of sexual pain in women, and current information regarding its assessment and treatment is needed.

**Aim:** To update the scientific evidence published in 2010, from the Third International Consultation on Sexual Medicine, pertaining to the assessment and treatment of women's sexual pain.

**Methods:** An expert committee, as part of the Fourth International Consultation on Sexual Medicine, was comprised of researchers and clinicians from biological and social science disciplines for the review of the scientific evidence on the assessment and treatment of women's genital pain.

**Main Outcome Measures:** A review of assessment and treatment strategies involved in vulvodynia.

**Results:** We recommend the following treatments for the management of vulvodynia: psychological interventions, pelvic floor physical therapy, and vestibulectomy (for provoked vestibulodynia). We also support the use of multidisciplinary treatment approaches for the management of vulvodynia; however, more studies are needed to determine which components are most important. We recommend waiting for more empirical evidence before recommending alternative treatment options, anti-inflammatory agents, hormonal agents, and anticonvulsant medications. Although we do not recommend lidocaine, topical corticosteroids, or antidepressant medication for the management of vulvodynia, we suggest that capsaicin, botulinum toxin, and interferon be considered second-line avenues and that their recommendation be revisited once further research is conducted.

**Conclusion:** A comprehensive assessment is needed to understand the pain experience of women presenting with vulvodynia. In addition, treatment typically progresses from less invasive to more invasive, and several treatment options are worth pursuing.

*J Sex Med* 2016;13:572–590. Copyright © 2016, International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

**Key Words:** Vulvodynia; Sexual Pain; Vestibulodynia; Assessment; Diagnosis; Treatment

## INTRODUCTION

A thorough assessment is necessary when a patient presents with vulvodynia (ie, chronic, idiopathic vulvar pain). There are

two main subtypes of vulvodynia: PVD (formerly called vulvar vestibulitis syndrome, focal vulvitis, vestibular adenitis, and focal vestibulitis vulvae), which is characterized as localized provoked pain at the vaginal vestibule, and generalized vulvodynia (GVD; formerly termed essential or dysesthetic vulvodynia and burning vulva syndrome), which is characterized by unprovoked, diffuse vulvar pain affecting the entire vulvar area.<sup>1</sup> Subgroups within these subtypes also can exist. For example, some studies on PVD have indicated that pain *onset* can be an important factor to consider. Indeed, the issue of whether the pain has been present since the patient's first episode of vaginal penetration (ie, lifelong or primary PVD, referred to as PVD1) or after a period of pain-free activities (ie, acquired or secondary PVD, referred to as PVD2) has been found by some to influence treatment outcome (eg, Heddini et al<sup>2</sup>; for a review of distinct and overlapping factors in PVD1 and PVD2, see Pukall<sup>3</sup>).

Ideally, a comprehensive evaluation of a woman with vulvodynia will consist of pain and medical histories and medical,

Received September 15, 2015. Accepted January 8, 2016.

<sup>1</sup>Department of Obstetrics and Gynecology, The George Washington University School of Medicine and Health Sciences, Washington, DC, USA;

<sup>2</sup>Department of Psychology, Queen's University, Kingston, ON, Canada;

<sup>3</sup>Department of Clinical Pharmacy, University of Tennessee Health Science Center, Memphis, TN, USA;

<sup>4</sup>Department of Psychology, Université de Montréal, Montréal, QC, Canada;

<sup>5</sup>Beyond Basics Physical Therapy, LLC, New York, NY, USA;

<sup>6</sup>Department of Obstetrics and Gynecology, Drexel University College of Medicine, Philadelphia, PA, USA;

\*Joint first-authorship.

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<http://dx.doi.org/10.1016/j.jsxm.2016.01.020>

## SUMMARY OF ALL RECOMMENDATIONS AND GRADES IN THIS ARTICLE

1. We recommend psychological interventions for the management of vulvodynia (grade B).
2. We recommend pelvic floor physical therapy for the management of vulvodynia (grade B).
3. We believe that there are not enough data to make an overall recommendation regarding alternative treatment options for the management of vulvodynia at this time (grade D), although acupuncture appears to be promising (grade C).
4. We believe that an interdisciplinary treatment approach is useful in the management of vulvodynia; however, further studies are necessary to determine the efficacy of this approach and to investigate which components are most important (grade C).
5. We do not recommend lidocaine as a long-term management option for provoked vestibulodynia (PVD; grade B).
6. We cannot recommend capsaicin as first-line treatment for PVD, but it can be considered if other treatments fail or as an alternative to more invasive surgery (grade C).
7. We do not recommend botulinum toxin A (BTA) as first-line treatment for PVD; however, we believe BTA can be considered second-line treatment for PVD until further clinical trials are conducted (grade C).
8. Owing to the lack of efficacy of low-dose corticosteroids and the potential side effects of high-potency corticosteroids, we do not recommend topical corticosteroids for the management of PVD (grade C).
9. Given the modest efficacy of the small non-controlled trials and lack of randomized controlled trials (RCTs) using interferon (INF) alone, we do not recommend INF as first-line treatment for the management of PVD (grade D).
10. Although the results of some very small RCTs are promising, larger studies are needed before anti-inflammatory agents can be recommended for treatment of PVD (grade D).
11. Although promising, further studies are needed before hormonal treatments can be recommended for treatment of PVD (grade C).
12. At this time, we recommend *against* the use of tricyclic antidepressant (TCA) medication for the management of PVD (grade A).
13. We recommend waiting for the results of an ongoing RCT before using anticonvulsant medication for the management of PVD (grade C).
14. We recommend vestibulectomy as a management option for PVD once other less invasive treatment options have been attempted (for most cases; grade B).

psychological, and pelvic floor muscle assessments. In this article, *genital pain* refers to the report of any kind of genital or abdominal pain (eg, from vulvodynia, chronic pelvic pain, or undiagnosed conditions); *vulvodynia* refers to the general condition of idiopathic, chronic vulvar pain; and *dyspareunia* indicates a common symptom of many genital pain conditions (including, but not limited to, vulvodynia; eg, chronic pelvic pain and pain during penetrative sexual activities). Because the condition of vulvodynia has only recently been formally recognized, there is very little level 1 evidence (eg, RCTs and meta-analyses) in this literature.

## ASSESSMENT

Because many aspects of women's overall health and well-being are affected by vulvodynia, a thorough assessment should involve a comprehensive evaluation of their pain history and medical, psychological, and pelvic floor muscle assessments. Throughout each step of the assessment, it is very important for the involved health care professional to use communication skills that enhance openness, comfort, trust, and confidence. Unfortunately, many women with vulvodynia will see several health care providers to comprehensively diagnose, evaluate, and decide on a management strategy.<sup>4</sup> As a result, women can feel patronized and marginalized from numerous prior unsuccessful

encounters, which can add to the burden. It is essential for each health care professional involved in a patient's care to address the woman's feelings to establish a constructive and trusting relationship and to allow enough time in the meeting to gain a complete picture of the presenting problem and the patient's experiences. If there is not enough time to focus on a specific complaint during a single visit, the patient should be reassured of the importance of her problem and scheduled for a follow-up appointment to address that issue alone.

Skills that can help health care professionals with establishing an optimal professional relationship with the patient are listed in [Table 1](#).

## Pain and Psychosocial Assessment

When a patient reports genital pain, a detailed pain and psychosocial history should follow.<sup>5</sup> Questions should cover, at a minimum, the following:

1. Pain characteristics, such as time since onset, temporal pattern, duration, location, quality, elicitors, and intensity, and whether the pain is primary or secondary
2. Musculoskeletal history, such as any surgery, injury, or falls to the lumbo-pelvic-hip region and/or the tailbone and sacrum
3. Bowel and bladder function history

**Table 1.** Suggested Skills for an Optimal Professional Relationship With a Patient

|   |
|---|
| Assure the patient of confidentiality and privacy   |
| Find a balance between being too formal and too informal during meetings  |
| Allow the patient to narrate her experience of the condition and be mindful of the sequential timeline of her disease process   |
| A patient likely will become emotional and there might be moments of silence, but this process can be cathartic for her; allowing her the space to express her feelings and to sit with silence conveys the message that she will not be rushed, ignored, or devalued in the clinician-patient relationship |
| Ask a mixture of closed- and open-ended questions while displaying empathy, understanding, and acceptance   |
| Consider patient requests for a support person to attend the meetings (although some history might not be disclosed with another person present, so it might be wise to set aside some individual time with the patient to query about any missing information)   |
| Communicate clearly and concisely to the patient  |
| Be mindful not to interrupt the patient's narrative   |
| Repeat some of the information back to the patient to confirm the accuracy of your understanding to her   |
| React in an appropriate manner (ie, in a calm, accepting, and professional manner) to the content of the discussion   |
| Offer the presence of a female chaperone during a pelvic examination performed by a male physician  |

4. Sexuality: desire, arousal, orgasm, frequency of and satisfaction with sex, sexual repertoire, and sexual distress
5. Thoughts, emotions, behaviors, and couple interactions that accompany the pain, in particular, avoidance behaviors, conflict and negative partner responses, pain attributions, catastrophizing, hypervigilance, fear of pain, self-efficacy (ie, the belief of one's own ability to achieve a goal), anxiety and depression, all of which can increase or decrease the pain
6. Comorbid medical or mental health conditions and treatments
7. Previous treatment attempts and outcomes
8. If relevant, current romantic relationship: strengths, areas of conflict including potential verbal and physical abuse, how they cope with the pain as a couple, emotional and non-sexual physical intimacy
9. Childhood trauma, including abuse and neglect, and any adult negative sexual experience
10. Validated self-report questionnaires (eg, Female Sexual Function Index [FSFI]<sup>6</sup>) can be useful for making comparisons with clinical norms or to track treatment progress

Characterization of the pain is crucial to determining the most successful path for management, because some treatments that would be appropriate for PVD (eg, vestibulectomy; see below) would not be recommended to women with GVD.<sup>7</sup> Typically, provoked pain during sexual activities involving vaginal penetration is the most common complaint of women with PVD. The pain of PVD is usually described as sharp and/or burning

and as localized to the vaginal entrance.<sup>8</sup> The typical presentation of a woman with GVD is quite different. She will usually complain of pain over the entire vulva that is constant or usually constant, and the pain can worsen when there is contact to the affected area. The pain of GVD is usually described as burning, irritating, and sore.<sup>9</sup>

## Assessment and Specific Outcome Measurements

### Assessment Measurements

Table 2 presents some of the most common validated measurements and suggested tools for assessing pain, mood (ie, depression, anxiety), sexuality, relationship adjustment, quality of life, childhood trauma, and treatment outcome.<sup>6,10–28</sup> At a minimum, the following domains should be assessed in vulvodynia outcomes studies: pain, emotional functioning, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, participant disposition (eg, adherence to the treatment regimen and reasons for premature withdrawal from the trial), and role and interpersonal functioning. This suggestion is based on recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials.<sup>29</sup>

### Capturing “Real-Time” Pain

**Cotton-swab test.** The cotton-swab test is the standard test for the diagnosis of PVD, the most common vulvodynia subtype, characterized by localized, provoked pain.<sup>30</sup> It consists of palpation of several genital regions, in particular the vulvar vestibule, with a cotton-tipped applicator. Different health care professionals perform this test in different ways; for example, some moisten the cotton-swab tip, whereas others do not, and some palpate in a consecutive order, whereas others palpate in a non-consecutive order. Moreover, health care professionals gauge pain by observing the patient's reactions, by asking a yes-or-no question, and/or by asking them to rate the intensity of the pain on a numerical rating scale (NRS). Although the cotton-swab test is useful for confirming an initial diagnosis, it is not a standardized method of assessment; it depends on the type, extent, and manner of pressure exerted by the person performing the test. However, if the study protocol involves the randomization of cotton-swab locations (see Pukall et al<sup>31</sup>) and the same tester, reporting method, and cotton-swab properties (eg, always using moistened tips with the same lubricant), the cotton-swab test can be useful for outcome studies (eg, Bergeron et al<sup>32</sup> and Goldfinger et al<sup>33</sup>).

**Vulvalgesiometer.** In 2004, Pukall et al<sup>31</sup> described the results of pressure-pain threshold testing (a type of quantitative sensory testing method) with a seven-set vulvalgesiometer in women with and without PVD. This device standardizes the amount of pressure applied to the vestibule to quantify levels of sensitivity. The standardization of pressure is important for some research goals because it has been demonstrated that when comparing cotton-swab pain intensity ratings of women with PVD between health care professionals, significant differences result, likely from the amount of

**Table 2.** Assessment Measurements

| Variable to be assessed               | Measurement   |
|---------------------------------------|---|
| Pain                                  | Numerical rating scale (NRS) of pain intensity (eg, from 0 = no pain at all to 10 = worst pain ever)  |
|                                       | McGill Pain Questionnaire (MPQ) <sup>10</sup>   |
|                                       | Pain Catastrophizing Scale (PCS) <sup>11</sup>  |
|                                       | Painful Intercourse Self-Efficacy Scale (PISES) <sup>12</sup>   |
|                                       | Vaginal Penetration Cognition Questionnaire (VPCQ) <sup>13</sup>  |
| Mood                                  | Vulvar Pain Functional Questionnaire (V-Q) <sup>14</sup> ; although the title of the questionnaire implies that this measurement assesses only vulvar pain, the individual items query only “pelvic” pain; thus, it might be worthwhile to discuss this discrepancy with patients who are responding to the questionnaire |
|                                       | Female National Institutes of Health Chronic Prostatitis Symptom Index (Female NIH-CPSI), adapted from the NIH Chronic Prostatitis Index (NIH-CPSI) <sup>15</sup>   |
| Depression                            | Beck Depression Inventory-II (BDI-II) <sup>16</sup>   |
|                                       | Center for Epidemiologic Studies Depression Scale (CES-D) <sup>17</sup>   |
|                                       | Patient Health Questionnaire (PHQ-8 <sup>18</sup> ; PHQ-9 <sup>19</sup> )   |
| Anxiety                               | State/Trait Anxiety Inventory (STAI) <sup>20</sup>  |
| Sexuality                             |   |
| Sexual function                       | Female Sexual Function Index (FSFI) <sup>6</sup>  |
| Sexual satisfaction                   | Global Measure of Sexual Satisfaction (GMSS) <sup>21</sup>  |
| Sexual distress                       | Female Sexual Distress Scale (FSDS) <sup>22</sup>   |
| Relationship adjustment               | Couple Satisfaction Index (CSI) <sup>23</sup>   |
|                                       | Dyadic Adjustment Scale (DAS) <sup>24</sup>   |
|                                       | Relationship Assessment Scale (RAS) <sup>25</sup>   |
| Quality of life and life interference | MOS 36-Item Short-Form Health Survey (SF-36) <sup>26</sup>  |
| Childhood trauma                      | Childhood Trauma Questionnaire (CTQ) <sup>27</sup>  |
| Treatment outcome                     | Patient Global Impression Change Scale (PGIC) <sup>28</sup>   |

pressure applied.<sup>31</sup> Pukall et al<sup>34</sup> simplified the design of the vulvalgesiometer to a set of five and increased the number of pressure levels to 26 (vs 24 with the seven-set vulvalgesiometer). Results indicated high inter-rater reliability between two testers, a significant between-groups (PVD and pain-free control women) difference of pressure-pain thresholds, and similar descriptors as those elicited with the seven-set vulvalgesiometer. The vulvalgesiometers

have been used in different studies including treatment outcome (eg, Goldfinger et al<sup>33</sup>).

**Tampon test.** The intensity of coital pain is considered the “gold standard,” but practical and methodologic difficulties arise because pain can be so intense that women might completely abstain from intercourse. The tampon test was tested as an innovative, alternative measurement of coital pain.<sup>35</sup> Preliminary data suggest that the tampon test might be an accurate, easily accessible, and cost-effective primary outcome measurement because of its limited participant burden and strong methodologic properties: it represents a real-life experience that has been shown to have excellent construct validity (its ratings [using a 0–10 NRS, where 0 = no pain and 10 = worst possible pain] correlate with intercourse and cotton-swab test pain ratings), discriminant validity (there is a lack of correlation with psychometric measurements, such as the Beck Depression Inventory and the Profile of Mood States), and test-retest reliability (consistent tampon test ratings over time).

## Medical Assessment

Despite the high prevalence of vulvodynia, there are few comprehensive guidelines regarding its comprehensive medical evaluation. The following section is an overview of the essential components of a thorough medical assessment: medical history, physical examination, and recommended laboratory tests.

## Medical History

Once the interview and pain assessment have been completed, it might be necessary to clarify the patient’s expectations. She might have several different complaints, so it will be important to determine which of these she feels is her chief complaint. For example, she might complain of generalized vulvar pain and burning, pain during intercourse, decreased libido, and difficulty achieving orgasm. For a complex clinical picture such as this one, it is likely that several concurrent and sequential treatments will be needed.

Once the chief complaint has been established, additional information should be gathered that might help the clinician narrow the differential diagnosis. Information related to medical, social, sexual, surgical, and medication histories is often essential to this process. Several tools can aid in gathering this information. The International Society for the Study of Vulvovaginal Disease has developed an extensive questionnaire that patients can fill out before their first appointment (this questionnaire is available online at <https://netforum.avectra.com/temp/ClientImages/ISSVD/3ef9c6ea-aac7-4d2b-a37f-058ef9f11a67.pdf>). A list of questions that might be valuable in the diagnosis of genital pain disorders is presented in Table 3.<sup>36</sup> The development of a validated instrument for chronic vulvar pain is currently ongoing.<sup>37</sup> Validated questionnaires also can be used to aid in the diagnosis of some genital pain disorders, including dyspareunia from endometriosis<sup>38</sup> and interstitial cystitis.<sup>39</sup> To assess sexuality-related issues, the FSFI (<https://www.fsf-questionnaire.com>) has been validated in women with chronic pelvic pain<sup>40</sup> and vulvodynia<sup>41</sup> and is commonly used. The FSFI is not

**Table 3.** Useful Questions to Ask When Obtaining a Sexual Pain History\*

|  |
|--|
| Do you have a history of:  |
| Physical, sexual, and emotional abuse or anxiety?  |
| Low back or hip pain?  |
| Urinary urgency, frequency, hesitancy, or incomplete emptying?   |
| Chronic constipation or rectal fissures?   |
| Oral contraceptive pill use (especially those with ethyl estradiol 20 µg or the progestins norgestimate or drospirenone) before or during onset of symptoms? |
| Ovarian suppression by Lupron or Depo-Provera?   |
| Decreased libido or decreased vaginal lubrication before the onset of dyspareunia?   |
| Perimenopausal or menopausal symptoms such as hot flashes and night sweats?  |
| Contact allergies or skin sensitive to chemicals?  |
| Recurrent (culture positive) yeast infections?   |
| Persistent yellowish vaginal discharge?  |
| Persistent white vaginal discharge?  |
| Severe burning or an allergic reaction to a topical medication on the vulva or vagina?   |
| Burning after intercourse?   |
| Avoidance of intercourse?  |
| Pain since first attempt at intercourse without any pain-free sex?   |
| Pain with first tampon use?  |
| Increased sensitivity of the umbilicus?  |
| Postcoital spotting or bleeding?   |
| Vulvar itching?  |
| Night-time scratching?   |
| Diarrhea?  |
| Midcycle spotting or pain?   |
| Worsening pain in a sexual position with deep thrusting?   |
| Vulvar ulcerations, tears, fissures?   |
| Painful periods?   |
| Chronic pelvic pain?   |
| Feeling an obstruction in the vagina?  |
| Pain beginning after childbirth?   |
| Dribbling after urination?   |
| Changes in coloration or architecture of the labia or vulva?   |
| Decreased clitoral sensation?  |
| Frequent bicycle riding?   |
| Aggressive abdominal muscle strengthening or Pilates?  |
| Pain mainly at the clitoris?   |
| Since pain during intercourse began, has there been any pain-free intercourse?   |
| If yes:  |
| Do you have oral lesions or bleeding gums?   |
| Do you have a history of high-risk human papillomavirus or cervical dysplasia?   |

\*Adapted from Goldstein.<sup>36</sup>

appropriate for women who have not been sexually active in the preceding 4 weeks; thus, it might not be the most appropriate measurement in women with dyspareunia because many affected women will avoid painful sexual activities.

### Medication History

Many medications have been associated with the patient report of vulvodynia. Therefore, it is essential to develop a timeline of medication use and compare it with the timeline of the patient's pain history. Because more than 90% of women take prescription medication, a discussion of the most commonly prescribed medications and their association with dyspareunia is warranted.<sup>42</sup> In addition, it is important to note that patients frequently do not disclose use of herbal supplements to clinicians; thus, it is important to ask the patient directly about herbs, vitamins, and alternative therapies during the medication history.

Antibiotics are the most common prescription medication in women.<sup>43</sup> Although antibiotics do not directly cause genital pain, long-term exposure can predispose women to chronic yeast infections, which have been associated with a higher than expected rate of vulvodynia (eg, Arnold et al<sup>44</sup>). Hormonal contraceptives (eg, oral contraceptives, transdermal patch, and vaginal ring) are the second most common prescription medication used by reproductive-age women.<sup>45,46</sup> It has been suggested that oral contraceptives contribute to PVD by decreasing free circulating testosterone, which might be harmful to the glands and endothelium of the vulvar vestibule.<sup>38</sup> Approximately 15% of reproductive-age women use psychotropic medications (prescription medications for anxiety and depression).<sup>47</sup> Although psychotropic medications are more frequently associated with clinical diagnoses of low desire and arousal in women than with diagnoses of genital pain, these features can contribute to dyspareunia because of their effects on vaginal lubrication.<sup>48</sup>

### Physical Examination

It is important to recognize that many women with dyspareunia will have high levels of anxiety in response to a physical examination involving an assessment of the external and internal pelvic structures. One study reported that one of the most common strategies used by physicians when examining patients who are uncomfortable with the internal pelvic examination is the interactive educational pelvic examination.<sup>49</sup> The educational pelvic examination consists of educating the patient about her anatomy while the steps of the examination take place and the rationale for the steps is explained. The patient is encouraged to observe the examination with a hand-held mirror and ask questions about her anatomy and the examination procedure. Conducting an educational pelvic examination is crucial to the success of the examination, because it has been demonstrated that women desire more information to be provided to them before and during pelvic examinations<sup>50</sup>; in addition, a negative experience with pelvic examinations has been found to correlate with a lack of knowledge on the part of the patient.<sup>50</sup>

The utility of a comprehensive and well-informed physical examination is invaluable. The physical examination can supplement self-reported history and correct misinformation from the patient and from a "quick-and-easy" approach to medical assessment. Although this examination focuses primarily on the

urogenital system, additional organ systems (eg, musculoskeletal or gastrointestinal) might need to be assessed depending on information gathered during the medical history. The goal of the physical examination is to gather data to help determine the etiology of vulvodynia and offer specific treatment for the pain. This goal requires a meticulous and methodical examination. In addition, the physical examination could play a key role in validating the patient's pain as "real" if the examiner can identify the correct location and by manual examination reproduce a woman's pain experience. This process can inspire patient confidence that the practitioner will be able to treat her pain.

**Colposcopic examination.** It can be useful for the patient to observe her physical examination to establish a common nomenclature (ie, naming standard) for parts of her urogenital system. A video colposcope or a hand-held mirror can allow the patient to visualize all aspects of the examination, should she wish to be involved in this way. Colposcopic examination of the vulva, commonly referred to as vulvoscopy, is very useful in the evaluation of women with vulvodynia. Important findings that can be observed at the visual examination of the vulva include infection, trauma, atrophy, dermatitis, and neoplasia. Specifically, the observer should note any inflammation, erythema, induration, excoriation, fissures, ulceration, lichenification, hypopigmentation, pallor, hyperpigmentation, scarring, or architectural changes, which might be evidence of dermatologic disease of the vulva.<sup>51</sup> Although erythema is a non-specific finding, intense redness at the ostia of the Bartholin and Skene glands is suggestive of PVD. Abnormalities identified at vulvoscopy might warrant vulvar punch biopsy examination.<sup>52</sup>

**Sensory examination.** A sensory examination of the vulva should be performed using a moistened cotton swab to determine whether there are areas that exhibit an abnormal pain response (ie, the cotton-swab test). This examination should be performed systematically to ensure that all areas of the anogenital region are investigated. Structures that are not midline should be palpated bilaterally. Initially, the medial thigh, buttocks, and mons pubis should be palpated. These areas are typically not painful, and this non-painful "practice" step can allow the patient to become comfortable with, and adapt to, the palpation method. Then, the labia majora, clitoral prepuce, perineum, and intra-labial sulci should be palpated. Pain in these areas suggests a process that is affecting the entire anogenital region (eg, vulvar dermatoses or vulvovaginal infections). Then, the labia minora should be gently palpated. The medial labia minora should be gently touched lateral to the Hart line, which is the lateral boundary of the vulvar vestibule. The cotton swab should be used to palpate the vestibule gently at five locations (however, non-adjacent palpation of these sites is recommended to decrease sensitization; see Pukall et al<sup>31</sup>): at the ostia of the Skene glands (lateral to the urethra), at the ostia of the Bartholin glands (4 and 8 o'clock at the vestibule), and at 6 o'clock at the fossa navicularis. Patients with PVD typically will experience allodynia

during cotton-swab palpation of the tissue of the vulvar vestibule, but they will perceive normal sensation lateral to the Hart line. If the pain is localized to the vestibule, then it is important to determine whether the pain affects the entire vestibule or just the posterior portion of vestibule; pain throughout the entire vestibule might be associated with an intrinsic pathology within the mucosa of the vestibular endoderm, whereas pain confined to the posterior vestibule suggests that the pain might be associated with a pathology extrinsic to the vestibule, most commonly hypertonic pelvic floor muscle dysfunction.<sup>53</sup>

**Speculum examination.** A speculum examination of the vagina is the next step. In general, a pediatric-size Graves speculum should be used and all efforts should be used to insert the speculum through the hymeneal ring without touching the vulvar vestibule. Initially, the vagina should be examined for evidence of abnormal vaginal discharge. A cotton swab should be used to collect some discharge for pH testing, wet mount, and potassium hydroxide (KOH) prep. In addition, a culture should be obtained and sent for speciation and sensitivity. Important findings while visualizing the vagina include atrophy (loss of rugae), erythema, erosions, ulcerations, abnormal discharge, or synechia. Then, a manual examination should be performed with one finger instead of the usual two fingers. During this examination, the examiner's index finger is inserted through the hymen without touching the vestibule. The urethra and bladder trigone should be gently palpated, followed by the levator ani muscles (see Assessment of the Pelvic Floor Musculature). The ischial spine should be located and the pudendal nerve should be palpated as it enters the Alcock canal. Next, a bimanual examination is performed to assess the uterus and adnexa (ovaries and fallopian tubes). A rectovaginal examination should be performed to assess the rectovaginal septum and posterior cul-de-sac.

## Testing

### Wet Mount and Cultures

Vaginal discharge should be examined by wet prep of the vaginal secretions (with KOH and saline) and pH testing of the vaginal vault. Specifically, vaginal discharge should be obtained on two cotton swabs from the upper third of the vagina, and the pH of the discharge should be tested. Because microscopic examination frequently misses candidiasis and trichomoniasis, a culture obtained at the time of vaginal inspection should be sent for speciation and sensitivity. In addition, if there is significant leukorrhea, a swab should be obtained for an immunochromatographic assay for trichomonas (Genzyme Corporation, Cambridge, MA, USA).

### Histology

As mentioned earlier, a vulvar or vaginal biopsy sample should be obtained if there are specific findings at visual inspection or colposcopic examination of the vulva suggestive of dermatoses, intraepithelial neoplasia, or neoplasia. However, it is unlikely that

the biopsy sample will prove useful if the physical findings are limited to non-specific erythema.

### Serum Testing

Serum hormone testing can be useful in women with vulvodynia. Because hormonal abnormalities can be involved in vulvodynia, blood should be obtained for serum estradiol, total testosterone, free testosterone, albumin, SHBG, follicle-stimulating hormone, and prolactin. Increased SHBG and decreased free testosterone and estradiol are frequently found in women with PVD who are on hormonal contraceptives.<sup>54</sup>

### Additional Testing

Referrals for additional investigations (eg, radiographic or ultrasonographic imaging, assessment of the pelvic floor musculature) should be based on findings during the history and physical examination given the complexity of factors involved in vulvodynia.

## Assessment of the Pelvic Floor Musculature

Chronic vulvar pain can indicate a wide range of musculoskeletal and neuromuscular problems that can occur when the muscles, nerves, and tissues of the pelvic floor and/or surrounding areas are restricted and overactive or when there is a dysfunction, dissymmetry, or misalignment in the skeletal system. Therefore, an assessment of the pelvic floor, trunk, and lower extremity musculature is advisable in patients presenting with vulvar pain. Indeed, several controlled studies have indicated that women with PVD have an increase in pelvic floor muscle tone (eg, Morin et al,<sup>55</sup> Gentilscor-Saulnier et al,<sup>56</sup> Reissing et al<sup>57</sup>), especially in the superficial level, and poorer pelvic floor muscle strength and control. These results suggest that the role of the pelvic floor muscles in the experience of vulvodynia is crucial to assess thoroughly.

A thorough evaluation of the pelvic floor muscles begins with a detailed pain assessment and medical history. Then, the patient's posture, alignment, gait patterns, and movement of the sacroiliac joint, spine, and hip are evaluated for dysfunction. In addition, limitations in range of motion and in the strength and joint integrity of the extremities must be evaluated. Next, palpation of the abdominal, gluteal, and back muscles, lower extremities, and pelvic floor muscles examines the presence of sensitive areas, shortened muscles, and pain (referred or local). Specific nerves that innervate the genital area—the posterior femoral cutaneous nerve that innervates the perineum, the pudendal nerve that innervates the inferior vagina and the perineum, the ilioinguinal and genitofemoral nerves that innervate the labia and mons pubis—should be assessed for allodynia, hyperpathia, and dysesthesia.<sup>58–60</sup>

Pelvic floor excursion testing, which should be performed visually and with biofeedback, objectively measures pelvic floor muscle coordination and the muscle's ability to relax by assessing contraction, relaxation, and bulge.<sup>61</sup> If the patient cannot relax or demonstrates incoordination in the pelvic floor, then this technique can demonstrate muscle overactivity. By using external

perianal pads or internal sensors, the therapist can teach the patient to relax or activate the muscles.<sup>62–64</sup> Positive findings will support the likelihood of bladder, bowel, and/or sexual dysfunction and abdominopelvic pain.<sup>65</sup>

## TREATMENT

The typical treatment plan for a woman with vulvodynia starts with treatments that are considered non-invasive (eg, psychological treatments, physical therapy) and, depending on her response to treatment, can progress to medical treatments (eg, gabapentin, topical hormones). If these treatments fail, then surgical intervention (if the pain is limited to the vestibule) can be recommended. Treatment progression is usually consecutive and based on “trial and error”<sup>66</sup>; however, King et al<sup>53</sup> recently suggested a more algorithmic approach based on physical examination findings and laboratory tests when deciding on specific treatments. Some have argued that starting with more invasive treatments, such as surgical intervention, should be considered because of its high effectiveness and low side effect profile,<sup>67</sup> and others have stated that concurrent or integrative (ie, multidisciplinary) treatments, if possible, might be more efficacious in outcome.<sup>68</sup>

### Non-Medical

Despite their widespread use in the multimodal treatment of other chronic pain conditions, non-medical treatments are sometimes absent from algorithms published in the medical literature. These treatments include psychotherapy, pelvic floor physical therapy, and alternative treatments.

#### Psychological Interventions (Level of Evidence = 2)

Psychological interventions focus on decreasing pain, restoring sexual function, and strengthening the romantic relationship by targeting the thoughts, emotions, behaviors, and couple interactions associated with the experience of genital pain. Such interventions can be delivered in individual, couple, or group formats. Cognitive-behavioral therapy (CBT) is the most commonly used and most studied psychological intervention to date. Bergeron et al<sup>69</sup> investigated the efficacy of a combination of group CBT in two different randomized trials of women with PVD. In their first study, which compared vestibulectomy, biofeedback, and CBT, participants who received CBT reported significant decreases in pain intensity during intercourse at a 6-month follow-up, from 7.1 before treatment to 4.5 on an NRS from 0 (no pain at all) to 10 (worst pain ever felt). In comparison, participants in the vestibulectomy and biofeedback conditions reported improved scores from 7.2 to 3.4 and from 6.9 to 4.5, respectively, with vestibulectomy participants showing significantly more pain decrease than that demonstrated in the other two treatment groups. However, at a 2.5-year follow-up, CBT participants' ratings of pain during intercourse were not significantly different from those of women having undergone a vestibulectomy (CBT = 3.3, vestibulectomy = 2.1). In another study, participants were randomly assigned to a

corticosteroid cream or to group CBT for a 13-week treatment period.<sup>70</sup> Intent-to-treat multilevel analyses showed that participants in the two groups reported statistically significant decreases in pain measurements from baseline to after treatment and 6-month follow-up, although the CBT group reported significantly greater pain decrease at 6-month follow-up on the six-point Present Pain Intensity scale of the McGill Pain Questionnaire (where 0 = no pain and 5 = excruciating; CBT = 3.6 before treatment to 2.6 at 6-month follow-up; corticosteroid cream = 3.5 before treatment to 3.1 at 6-month follow-up). After treatment, women in the CBT condition were significantly more satisfied with their treatment, displayed significantly less pain catastrophizing, and reported significantly better global improvements in sexual functioning than women assigned to the topical application. Findings suggest that CBT might have a positive impact on more dimensions of genital pain than a topical treatment. Other studies have demonstrated the effectiveness of psychological interventions for vulvodynia (eg, Masheb et al,<sup>71</sup> Corsini-Munt et al,<sup>72</sup> Brotto et al<sup>73</sup>). Overall, individual and group psychological treatments represent empirically validated, non-invasive, and safe therapeutic options for genital pain, whereas couple interventions remain to be rigorously assessed (for a comprehensive review of treatments for genital pain, see Al-Abbadey et al<sup>74</sup>). Therefore, we recommend psychological interventions for the management of vulvodynia (grade B).

#### Pelvic Floor Physical Therapy (Level of Evidence = 3)

Women with vulvodynia usually exhibit hypersensitivity and tenderness of the pelvic floor muscles because of shortening, inflammation, altered perfusion, and neural patterns. Pelvic floor physical therapy for vulvodynia uses pelvic and core mobilization and stabilization techniques; connective tissue, visceral, and neural mobilization; internal and external myofascial trigger point release; and modalities such as biofeedback and electrical stimulation<sup>65,75</sup> to assist in decreasing tender points and decrease tissue restrictions. Subsequently, pelvic floor physical therapy assists in restoring the proper length of the pelvic floor muscles and tissues, decreasing neural tension, and decreasing dyspareunia.<sup>76–80</sup> Particular techniques of pelvic floor physical therapy are described below.

**Myofascial release and other manual techniques.** After a comprehensive assessment, the pelvic floor physical therapist can begin with manual connective tissue manipulation and myofascial trigger point release. These techniques are used to decrease restrictions in tissue, muscles, and nerves and to improve circulation to areas with decreased blood flow or pelvic congestion. These manipulation techniques increase motion in the tissues and facilitate mobility of the structures within the bony pelvis. Fitzgerald and Kotarinos<sup>78</sup> underscored the importance of repeated connective tissue and scar release until tissue adherence releases. In addition to external tissue release and core stabilization, direct internal transvaginal and transrectal release of myofascial trigger points in the pelvic floor muscles is a central aspect of pelvic floor physical therapy and sexual rehabilitation.<sup>81,82</sup> Manual therapy techniques, such as joint and scar tissue

mobilization and neuromuscular re-education, are applied to decrease tissue adherence and restore proper skeletal alignment and muscle memory. These interventions allow women to sit more comfortably, to participate in work and home activities more readily, and to benefit from improved bladder, bowel, and sexual function. Pelvic floor physiotherapists also re-educate patients through proprioceptive neuromuscular facilitation, verbal cuing, and biofeedback. Such re-education helps patients coordinate and down-train overactive muscles and constitutes an important adjunct to the manual techniques.<sup>77,78,83</sup>

**Stretching and strengthening.** A crucial aspect of pelvic floor and sexual rehabilitation is physical therapist-assisted stretching of the muscles of the back, lower extremities, and abdomen in addition to nerve gliding to facilitate movement in restricted nerves. The pelvic floor physical therapist augments stretching exercises with strengthening techniques that address muscle weakness, allowing for balance and stability. Education regarding the progression and rate of strengthening is important because trigger points and restricted neural and connective tissue can become more irritated if these techniques are initiated prematurely.<sup>60,81</sup>

**Physical therapy home program and behavioral modifications.** As part of pelvic floor rehabilitation, the physical therapist develops a “home program” that can include abdominal, hip, pelvic, lower extremity, and back stretching; daily relaxation and breathing exercises; patient-performed manual techniques on external and internal tissue; and bladder and bowel retraining as indicated.<sup>77,78</sup> Vaginal dilators can be recommended to normalize the tone of the muscles, desensitize hypersensitive areas of the vulva and vagina, and restore sexual function.<sup>84</sup> When needed, techniques such as guided imagery and mindfulness meditation can be incorporated into the patient’s home program to facilitate neural downregulation. Learning relaxation, self-release, and gentle strengthening techniques can empower patients and instill confidence.<sup>85</sup> In addition, behavioral training techniques can be incorporated into a program for the patient so that sexual rehabilitative efforts can be continued at home between therapy sessions. An individual who has experienced changes in bladder and bowel function can be given additional specific exercises to help these functions return to normal.<sup>65</sup>

**Manual physical therapy for pelvic pain: research findings.** Manual techniques, mobilization, and stabilization exercises are the core of pelvic floor physical therapy. The guidelines of the American Urological Association for the management of pelvic pain recommend manual physical therapy by clinicians appropriately trained in treating pelvic floor dysfunction and overactivity—in addition to the avoidance of improper pelvic floor strengthening exercises (ie, Kegels)—as essential treatment components.<sup>86</sup> Several studies have supported the efficacy of (components of) pelvic floor physical therapy for women with vulvodynia. For example, success rates of approximately 50%



were reported in two early studies involving electromyographic (EMG) biofeedback.<sup>87,88</sup> In addition, Danielsson et al<sup>89</sup> compared EMG biofeedback with topical lidocaine in the treatment of PVD.<sup>89</sup> Results indicated improvement in 12 of 18 patients (66%), which was maintained at the 12-month follow-up and was not significantly different from the women who received the lidocaine treatment. This randomized study indicated that 4 months of treatment with biofeedback or topical lidocaine resulted in significant improvements in vestibular pain, sexual function, and quality-of-life measurements. For example, on a visual analog scale assessing most recent intercourse pain intensity from 0 (best possible) to 100 (worst possible), Danielsson et al<sup>89</sup> reported significant changes in ratings from 74 to 42 from the first to fourth visits for the lidocaine treatment group. In addition, a randomized trial conducted by Bergeron et al<sup>32</sup> compared group CBT with EMG biofeedback and vestibulectomy as treatment modalities for women with PVD. On an NRS from 0 (no pain at all) to 10 (worst pain ever felt), CBT participants reported pain decreases from 7.1 before treatment to 4.5 at 6-month follow-up; vestibulectomy participants reported decreases from 7.2 to 3.4; and biofeedback participants reported decreases from 6.9 to 4.5, with vestibulectomy participants showing significantly greater pain decreases than the other two treatment groups. The average decrease in pain for biofeedback was 35%, and this was maintained at 2.5-year follow-up.<sup>69</sup>

More recent studies have focused less on the sole use of EMG feedback as a treatment for PVD and have provided evidence for the effectiveness of comprehensive pelvic floor physical therapy programs, which typically include EMG. In 2002, Bergeron et al<sup>90</sup> reported on a retrospective consecutive case investigation of the usefulness of six to eight sessions of manual pelvic floor physical therapy and adjunctive techniques, including education, biofeedback, electrical stimulation, and home programs, in the treatment of PVD. Approximately 71% of women with PVD reported moderate to complete improvement in pain at follow-up. For intercourse pain intensity ratings, women reported significant decreases from before to after treatment (from 8.2 to 3.9) on an NRS from 0 (no pain at all) to 10 (worst pain ever felt). Dionisi et al<sup>91</sup> observed improvement in pain in 110 (75.8%) of 145 patients with vulvodynia after 10 weekly sessions of physical therapy and electrical stimulation, biofeedback, and home therapy with stretching exercises of the pelvic floor. The results of the study suggest that these treatment techniques for pelvic floor relaxation are safe and effective in relieving vulvar pain and dyspareunia in women with vulvodynia.

In a prospective study involving 11 participants with PVD, Gentilcore-Saulnier et al<sup>56</sup> reported that a physical therapy program, consisting of components such as manual therapy and pelvic floor EMG techniques, led to normalization of the pelvic floor. A significant decrease in pain during vaginal palpation also was found, and participants reported significant decreases in pain during intercourse and during a gynecologic examination and improved sexual function.<sup>33</sup> Specifically, intercourse pain

intensity (rated on an NRS from 0, no pain at all, to 10, worst pain ever felt) decreased significantly from before treatment (6.73) to after treatment (2.23) and follow-up (2.27). From this brief review, treatment of the pelvic floor muscles is often a key element toward alleviating discomfort and restoring bladder, bowel, and sexual function. Although more prospective studies are warranted, pelvic floor physical therapy options appear to be effective for PVD. Therefore, we recommend pelvic floor physical therapy for the management of vulvodynia (grade B).

### Alternative Treatments (Level of Evidence = 3)

Some patients use alternative treatments (eg, acupuncture or hypnotherapy) for vulvodynia, although there are less data supporting their efficacy. Two uncontrolled prospective pilot studies showed that participants reported improvements in pain and sexuality after taking part in acupuncture<sup>92</sup> and hypnosis.<sup>93</sup> Recently, the first randomized wait-list controlled pilot study examining the use of acupuncture in women with vulvodynia was published.<sup>94</sup> Thirty-six women with vulvodynia were randomly assigned to the acupuncture or the wait-list control group. Results indicated that, after treatment, women who received acupuncture reported significantly less vulvar pain and dyspareunia and improvements in overall sexual function compared with the control group. Because these options are devoid of adverse effects, more rigorous studies are warranted. However, we believe there are not enough data to make an overall recommendation regarding alternative treatment options for the management of vulvodynia at this time (grade D), although acupuncture appears to be promising (grade C).

### Interdisciplinary Treatments (Level of Evidence = 3)

There are only two published uncontrolled quantitative studies evaluating a multimodal approach to the treatment of genital pain, and these reported major improvements in women's sexual function and pain.<sup>95,96</sup> These multimodal treatments integrated sex therapy and physical therapy in a non-standardized manner, such that not all participants received the same combination and duration of interventions. A retrospective qualitative study of 29 women with vulvodynia who participated in a multidisciplinary treatment program suggested that 27 reported a significant benefit, with 9 being pain free.<sup>97</sup> This program consisted of psychotherapy, physical therapy, and dietary advice. Another study using the same design was conducted in 19 women with vulvodynia who participated in a multimodal treatment that involved group CBT, physical therapy, and regular medical appointments. Results indicated that participants reported increased knowledge and tools to manage the pain, improved psychological well-being, a sense of validation and support, and an enhanced sense of empowerment.<sup>98</sup> Although only a few studies have examined interdisciplinary management options in the vulvodynia literature, the preliminary results seem promising. Therefore, we believe that an interdisciplinary treatment approach is useful in the management of vulvodynia; however, further studies are necessary to determine the efficacy of

this approach and to investigate which components are most important (grade C).

### Medical: Non-Surgical Options

Vulvodynia has many possible medical treatments, but very few controlled trials have been performed to verify the efficacy of these treatments. This section focuses on the use of topical antinociceptive agents (anesthetics, capsaicin, and botulinum) and topical anti-inflammatory agents (corticosteroids, INF, cromolyn, and lysate) in the treatment of PVD. Mechanisms of action, appropriate management, and level of evidence suggesting their efficacy are reviewed.

#### Antinociceptive Agents

**Local anesthetics (level of evidence = 2).** Local anesthetics exert their analgesic activity with the blockade of sodium channels on peripheral nociceptors and by blocking transmission of discharges from peripheral sensory nerves.<sup>99</sup> Sensitization of the peripheral vestibular nerves has been suggested as a possible mechanism of the pain in PVD.<sup>100</sup> Therefore, the theory behind the use of local anesthetics is to achieve long-lasting desensitization of the vestibular nerves. Table 4 presents details of studies investigating the efficacy of topical lidocaine, local anesthetic injections, and submucosal infiltrations of lidocaine combined with corticosteroids in women with PVD. Because the only double-blinded RCT using lidocaine failed to show any benefit and most non-controlled trials showed efficacy in the range of only 50%, we do not recommend lidocaine as a long-term management option for PVD (grade B).

**Capsaicin (level of evidence = 3).** The rationale for the use of capsaicin in the treatment of vulvodynia is based on increased vanilloid receptor (VR1) innervation found in women with this condition<sup>101</sup> and the agonist effects of capsaicin on vanilloid receptors located in the peripheral terminals of nociceptors.<sup>102</sup> After hyperesthesia to the initial exposure, capsaicin produces a long-lasting desensitization to burning and pain.<sup>102</sup> One prospective and one retrospective case series evaluated the efficacy of capsaicin cream in PVD (Table 4). However, in these studies, lidocaine was given before the capsaicin to prevent irritation or burning on administration, so it is impossible to isolate the effect of capsaicin. Because there have only been two uncontrolled studies on capsaicin, we cannot recommend capsaicin as first-line treatment for PVD, but it can be considered if other treatments fail or as an alternative to more invasive surgery (grade C).

**Botulinum type A (level of evidence = 2).** BTA (Botox) inhibits the release of glutamate and substance-P from nociceptive neurons.<sup>103</sup> Current hypotheses suggest that the inhibition of these nociceptors can decrease peripheral and central sensitization associated with vulvodynia. Although extremely rare, distant spread of botulinum toxin beyond the site of injection has been

reported, resulting in dysphagia and breathing difficulties and can be life threatening. The efficacy of BTA has been evaluated in one double-blinded placebo-controlled RCT, two case series, and two case reports (Table 4), with sites of injection depending on the study (the bulbospongiosus [perineal area] or the levator ani under EMG guidance). In summary, the one RCT of BTA showed no improvement compared with placebo, yet the non-controlled studies showed very significant efficacy. Therefore, we do not recommend BTA as first-line treatment for PVD; however, we believe that BTA can be considered second-line treatment for PVD until further clinical trials are conducted (grade C).

#### Anti-inflammatory Agents

**Corticosteroids (level of evidence = 2).** Tissue levels of interleukin- $\beta$  have been reported to be significantly higher in the hymen region of the vestibule of women with PVD,<sup>104</sup> and corticosteroids decrease the production of interleukin- $\beta$ ,<sup>105</sup> thus explaining their proposed mechanism. Table 5 presents a summary of studies investigating the use of anti-inflammatory agents in PVD. These data suggest that topical corticosteroids are minimally effective in treating PVD. It is unclear whether submucosal infiltrations of lidocaine combined with corticosteroids<sup>106–108</sup> are effective because no RCTs have been conducted. Therefore, owing to the lack of efficacy of low-dose corticosteroids and the potential side effects of high-potency corticosteroids, we do not recommend topical corticosteroids for the management of PVD (grade C).

**Interferon (level of evidence = 2).** INF is approved for the treatment of condylomata acuminata (genital warts). It downregulates the expression of proinflammatory cytokines<sup>109</sup> and is theorized to be effective in PVD because tissue levels of cytokines have been reported to be significantly higher in the hymeneal region of the vestibule of patients with PVD.<sup>85</sup> In addition, INF is a potent mast cell inhibitor, and it has been suggested that mast cells have a role in the initiation of PVD.<sup>110</sup> One RCT, three case series, and one case study examined the efficacy of INF in PVD (Table 5). Most of these studies found a modest improvement with submucosal vestibular INF injections. Further studies are necessary to determine whether INF alone or combined with surgery is an effective treatment for PVD. Given the modest efficacy of the small non-controlled trials and lack of RCTs using INF alone, we do not recommend INF as first-line treatment for the management of PVD (grade D).

**Other agents with anti-inflammatory properties (level of evidence = 2).** In a double-blinded, placebo-controlled RCT of 34 women with PVD, Nyirjesy et al<sup>111</sup> found that 53.8% (n = 7 of 13) of women receiving cromolyn cream, a mast cell stabilizer, compared with 38.5% (n = 5 of 13) of those receiving placebo cream had at least 50% improvement in dyspareunia and vestibular tenderness. In a double-blinded, placebo-controlled

**Table 4.** Evidence Summary Table of Antinociceptive for Vulvodynia

| Reference                                | Patient characteristics and study type   | Intervention and length of FU   | Outcome measurements                              | Results   | Evidence |
|--|--|---|---|---|----------|
| Foster et al, 2010 <sup>124</sup>        | DB PBO-controlled RCT (N = 133, 112 completed study), PVD, 18–50 y old                                   | Topical 5% lidocaine cream, oral desipramine 150 mg, lidocaine cream + oral desipramine, and matching PBO; 52-wk FU             | Tampon test, NRS, pain score, ISS                 | Tampon test score (decreases): PBO (33%), lidocaine cream (20%), desipramine (24%), lidocaine cream + desipramine (36%); sexual satisfaction improved with desipramine  | 1        |
| Petersen et al, 2009 <sup>125</sup>      | DB PBO-controlled RCT (N = 64, 60 completed study), PVD, 30.0 ± 6.19 y old                               | Botulinum toxin A injection (100 U), 6-mo FU  | Pain VAS 10-point Likert scale, FSFI, FSDS, SF-36 | 2 groups showed improved VAS scores, QOL and FSFI, PBO group had greater improvement in sexual distress   | 1        |
| Pelletier et al, 2011 <sup>126</sup>     | Case series (prospective; N = 20, all completed study), PVD, 18–24 y old                                 | Botulinum toxin A injection (100 U), 6-mo FU  | VAS, DLQI, FSFI                                   | 80% of patients showed improvement in pain after 3 and 6 mo; significant improvement in QOL and sexual function during first 6 mo; 70% could have sexual intercourse after 3 mo                                       | 2        |
| Danielsson et al, 2005 <sup>127</sup>    | RCT (N = 46, 37 completed study), PVD, 18–36 y old   | Topical 5% lidocaine ointment vs EMG, 12-mo FU  | Vulvar algesiometer, VAS, SF-36, QOL              | EMG: 2 of 18 completely cured, 12 of 18 improved, 3 of 18 no change, 1 missing; lidocaine: 2 of 19 completely cured, 10 of 19 improved, 3 of 19 no change, 4 missing; similar improvement in all outcome measurements | 2        |
| Zolnoun et al, 2003 <sup>128</sup>       | Case series (prospective; N = 69, 61 completed study), PVD, 24–36 y old                                  | Lidocaine 5% ointment, 6–8 wk and ≥6-mo FU  | Dyspareunia (VAS, 0–100 mm)                       | Dyspareunia decrease of ≥50% in 33 of 61; 25 of 61 did not reach this level   | 2        |
| Rapkin et al, 2008 <sup>129</sup>        | Case series (prospective; N = 27, all completed study), PVD, 35.9 ± 12.4 y (pre- and postmenopausal)     | Caudal epidural, pudendal, and vulvar injections of local anesthetics (ropivacaine, bupivacaine), 5 treatment sessions, 6-mo FU | Vulvalgesiometer, MPQ, FSFI, self-report          | Responders (≥50% decrease in score): MPQ 44.4%, algesiometer 40.7%, self-report 55.6%; significant improvement on FSFI in pain domain   | 2        |
| McDonald and Rapkin, 2012 <sup>130</sup> | Case series (prospective; N = 32, 26 completed study), vulvodynia, 18–65 y old (pre- and postmenopausal) | Caudal epidural, pudendal, and vulvar injections of local anesthetics (ropivacaine, bupivacaine), 5 treatment sessions, 3-mo FU | MPQ, BDI, FSFI                                    | Responders (≥50% decrease in score): MPQ 43%; significant improvement on BDI but not FSFI   | 2        |
| Murina et al, 2001 <sup>106</sup>        | Cases series (prospective; N = 22, 19 completed study), PVD, 19–44 y old                                 | Lidocaine and methylprednisolone submucosal infiltrations, up to 24-mo FU   | Dyspareunia, pain on cotton-swab test (0–3 scale) | 68.4% showed some improvement, 32% had complete improvement   | 2        |

(continued)

Table 4. Continued

| Reference                                | Patient characteristics and study type                                     | Intervention and length of FU   | Outcome measurements  | Results   | Evidence |
|--|--|---|---|---|----------|
| Murina et al, 2004 <sup>131</sup>        | Case series (prospective; N = 33, 32 completed study), PVD, 21–55 y old    | Capsaicin cream 0.05% (preceded by lidocaine + prilocaine) before administration, up to 6-mo FU | VAS for irritation or burning, dyspareunia (0–3 scale)                | Improvement in 19 of 32, no improvement in 13 of 32   | 2        |
| Steinberg et al, 2005 <sup>132</sup>     | Case series (retrospective; N = 52, 47 completed study), PVD, 20–41 y old  | Capsaicin cream 0.025% (preceded by 5% lidocaine gel before administration), up to 18-wk FU     | Kaufman touch test, Marinoff dyspareunia scale (1–3)                  | Significant improvement on touch test and Marinoff scales (absolute numbers not reported)   | 3        |
| Dystra and Presthus, 2006 <sup>133</sup> | Case series (retrospective; N = 19, all completed study, PVD, 23–51 y old) | Botulinum toxin A (35 U in 7 patients, 50 U in 12 patients); up to 14-wk FU                     | Self-reported pain (VAS 0–10), oral pain medication use, QOL          | Patients receiving 35 U had significant pain decrease for 8 wk; those receiving 50 U had decrease for 14 wk; significant improvement in pain medication use and QOL in all patients | 3        |
| Romito et al, 2004 <sup>134</sup>        | Case study (N = 2), PVD, 41 and 43 y old                                   | Botulinum toxin A injection (80 U for 1 patient and 40 U for other patients), up to 6-mo FU     | Dyspareunia (VAS 0–5)   | 2 of 2 had complete relief from pain and hypertonia of pelvic floor muscles for up to 6 mo  | 4        |
| Brown et al, 2006 <sup>135</sup>         | Case study (N = 2), PVD, 24 and 43 y old                                   | Botulinum toxin A injection (20 U at baseline, 40 U 12 wk later); up to 24-wk FU                | Dyspareunia (VAS 0–10), EMG measuring muscle hypertonicity, algometer | Coital pain decreased in 1 patient, pelvic floor hypertonicity decreased in 2 patients, negligible changes in vestibular hyperalgesia   | 4        |
| Dede et al, 2006 <sup>107</sup>          | Case study (N = 1), vulvodynia, 42 y old                                   | Lidocaine and betamethasone submucosal infiltrations, up to 6-wk FU                             | Subjective report   | Total relief from pain  | 4        |
| Segal et al, 2003 <sup>108</sup>         | Case study (N = 1), PVD, 24 y old  | Lidocaine and betamethasone submucosal infiltration for 6 wk, up to 12-mo FU                    | Not reported  | Total relief from pain and good quality of sex life   | 4        |

ASFQ = Abbreviated Sexual Function Questionnaire; BDI = Beck Depression Inventory; DB = double-blinded; DLQI = Dermatology Life Quality Index; EMG = electromyographic biofeedback; FSDS = Female Sexual Distress Scale; FSFI = Female Sexual Function Index; FU = follow-up; ISS = Index of Sexual Satisfaction; MPQ = McGill Pain Questionnaire; NRS = numerical rating scale; PBO = placebo; PVD = provoked vestibulodynia; QOL = quality of life; RCT = randomized controlled trial; SF-36 = 36-item short-form health survey; VAS = visual analog scale.

RCT of 26 women with PVD, Donders and Bellen<sup>112</sup> found that a skin cream that included the lysate of fetal fibroblasts—which contained different anti-inflammatory cytokines—produced a significant, although modest, decrease in vestibular sensitivity and intercourse pain than placebo cream. In a double-blinded, randomized placebo-controlled trial of 40 women, Farajun et al<sup>113</sup> used enoxaparin—a low-molecular-weight heparin with anti-heparinase properties—for the treatment of PVD. The enoxaparin-treated women showed a greater decrease in vestibular sensitivity at the end of treatment and 3 months later, and 75% (15 of 20) reported a decrease of pain greater than 20% compared

with 27.8% (5 of 18) in the placebo group. Although the results of these very small RCTs are promising, larger studies are needed before these agents can be recommended for the treatment of PVD (grade D).

**Hormonal treatments (level of evidence = 2–3).** In a non-placebo-controlled study, Burrows and Goldstein<sup>45</sup> found that a topical cream that combined estradiol 0.01% and testosterone 0.1% decreased visual analog pain scores from 7.5 to 2.0 in 50 consecutive women with PVD in whom the initiation of

**Table 5.** Evidence Summary Table of Anti-inflammatory Agents for Vulvodynia

| Reference                                | Patient characteristics and study type  | Intervention and length of FU   | Outcome measurements  | Results  | Evidence |
|--|---|---|---|--|----------|
| Munday et al, 2004 <sup>136</sup>        | DB RCT crossover (N = 22, 15 completed $\geq$ 1 arm of study), PVD                  | Potent steroid (clobetasol propionate 0.05%) vs mild steroid (hydrocortisone 0.5% ointment), 2-wk FU          | Pain, tenderness, erythema scales (0–3)   | Potent steroid: 11 of 15 with improvement, 2 of 15 unchanged, 2 of 15 worse; mild steroid: 9 of 15 with improvement, 1 of 15 no change, 5 of 15 worse                                    | 1        |
| Nyirjesy et al, 2001 <sup>111</sup>      | DB RCT (N = 34, but 8 deemed non-evaluable), PVD, 24–49 y old                       | Cromolyn cream 4% and PBO cream, 3-mo FU  | Symptom scale, dyspareunia scale (0–3), vestibular erythema and tenderness            | Treatment group: 7 of 13 with $\geq$ 50% decrease in symptoms; PBO group: 5 of 13 with $\geq$ 50% decrease in symptoms   | 1        |
| Donders and Bellen, 2012 <sup>112</sup>  | DB PBO-controlled RCT (N = 30, 26 completed trial), PVD, 18–55 y old                | Cutaneous lysate skin cream vs PBO cream; no FU   | CST (0–10), Von Frey filaments, vulvar erythema scale (0–4), dyspareunia scale (0–10) | Significant decrease in dyspareunia and erythema after 4 and 12 wk with active treatment but not with PBO; no group differences in CST and vulvar tactile threshold                      | 1        |
| Desrochers et al, 2010 <sup>137</sup>    | RCT (N = 111, 97 completed study), PVD, 18–45 y old                                 | 1% corticosteroid cream vs CBT, 6-mo FU   | VAS (0–10), MPQ, FSFI, STAI, PASS-20, PCS-SF  | Significant improvement in pain and sexual function with cream and CBT after treatment and at FU; CBT group showed significantly less catastrophizing and greater treatment satisfaction | 2        |
| Brown et al, 2009 <sup>138</sup>         | RCT (N = 53, 43 completed study), generalized and localized vulvodynia, 20–75 y old | Amitriptyline (10–20 mg) vs amitriptyline + 0.1% triamcinolone cream vs self-management, no post-treatment FU | MPQ   | No difference between groups on qualitative component of MPQ; self-management showed modest improvement on quantitative component  | 2        |
| Marinoff et al, 1993 <sup>139</sup>      | Case series (prospective; N = 55), PVD  | Interferon- $\alpha$ intralesional $\pm$ surgery (in non-responders)  | Introital dyspareunia subjective  | Interferon: 27 of 55 had substantial or partial improvement; interferon + surgery: 18 of 19 who had surgery had substantial or partial improvement                                       | 2        |
| Kent and Wisniewski, 1990 <sup>140</sup> | Case series (retrospective; N = 8), PVD   | Interferon- $\alpha$ , intralesional, >4-wk FU  | “Complete remission”  | 5 of 8 patients in remission; 1 of 8 with transient improvement and relapse after therapy ceased   | 3        |

(continued)

Table 5. Continued

| Reference                            | Patient characteristics and study type  | Intervention and length of FU  | Outcome measurements | Results   | Evidence |
|--------------------------------------|---|--|----------------------|---|----------|
| Bornstein et al, 1993 <sup>141</sup> | Case series (retrospective; N = 7), PVD | Interferon-beta IM (30–45 IU), up to 18-mo FU  | “Complete remission” | 45 IU: 3 of 3 were asymptomatic; 30 IU: 2 of 4 were asymptomatic, 2 of 5 did not show complete remission              | 3        |
| Bornstein et al, 1991 <sup>142</sup> | Case study (N = 1), PVD                 | Interferon-beta IM, 2-mo FU  | “Cure”               | Cured   | 3        |
| Bornstein et al, 1997 <sup>143</sup> | RCT (N = 19), PVD, 18–42 y old          | Total perineoplasty vs subtotal perineoplasty + interferon-alfa2b infiltration, up to 1-y FU | Not reported         | Total perineoplasty: 6 of 9 had complete response; subtotal perineoplasty + interferon: 7 of 10 had complete response | 4        |

BPI = Brief Pain Inventory; CBT = cognitive-behavioral therapy; CST = cotton-swab test; DB = double-blinded; FSFI = Female Sexual Function Index; FU = follow-up; IM = intramuscularly; MPQ = McGill Pain Questionnaire; PASS-20 = Pain Anxiety Symptom Scale; PBO = placebo; PCS-SF = Pain Catastrophizing Scale; PVD = provoked vestibulodynia; RCT = randomized controlled trial; STAI = Spielberger State-Trait Anxiety Inventory; VAS = visual analog scale.

combined oral contraceptive pills was associated with PVD onset. In an RCT, Foster et al<sup>114</sup> found that topical estradiol decreased vulvar pain sensitivity in menopausal women with mixed vulvovaginal complaints. Yount et al<sup>115</sup> reported that 88% of 201 women treated with topical estradiol alone or in combination with biofeedback had at least a 70% decrease in their pain. Although promising, further studies are needed before hormonal treatments can be recommended for the treatment of PVD (grade C).

### Systemic Medications

Leo and Dewani<sup>116</sup> conducted a literature review on the effectiveness of oral antidepressant medication in treating vulvodynia (level of evidence = 2). Their review included two RCTs, one quasi-experimental trial, seven non-experimental studies, and three case reports. Most patients discussed in the reports reviewed received TCA treatment. The results of RCTs of systemic TCAs provide evidence that they should not be used for PVD. Therefore, at this time, we recommend *against* the use of TCA medication for the management of PVD (grade A).

Anticonvulsant therapy has been recommended in the treatment of vulvodynia. However, convincing evidence to support this therapeutic option is lacking. Spoelstra et al<sup>117</sup> performed a review of the available peer-reviewed literature, including two case reports, three retrospective studies, two non-randomized prospective studies, and one open-label pilot trial study (level of evidence = 3); they recommended waiting for the results of an NIH-funded multicenter RCT to be completed before recommending the use of anticonvulsants for vulvodynia.<sup>118</sup> Therefore, at this time, we recommend waiting for the results of the ongoing RCT before using anticonvulsant medication for the management of PVD (grade C).

### Medical: Surgical

#### Surgical Options Focusing on the Vulvar Vestibule (Level of Evidence = 2)

It is well established that surgical treatment of PVD is the most effective medical strategy to decrease the pain. In 1981, Woodruff and Poliakoff<sup>119</sup> were the first to describe vulvar vestibulectomy. Their procedure consisted of the excision of a semicircular segment of perineal skin, the mucosa of the posterior vulvar vestibule, and the posterior hymeneal ring. Three centimeters of the vaginal mucosa was undermined and approximated to the perineum. Several variations of this procedure have since been described to help decrease complications, such as dehiscence of the vaginal advancement flap, and to improve operative success. A complete vulvar vestibulectomy with vaginal advancement includes excision of the mucosa of the entire vulvar vestibule including the mucosa adjacent to the urethra, whereas a modified vestibulectomy limits excision of the mucosa to the posterior vestibule.<sup>120</sup> However, it is important to note that surgical studies are difficult to compare, and they are typically not controlled.

Techniques and terminology used to describe the various procedures vary significantly. Different investigators have referred to widely different surgeries characterized by the same name. Often there are changes to the techniques used even in the same series of patients. The outcome criteria for “surgical success” are often poorly defined and rarely are standard procedures used to assess success. The evaluation of success is typically non-blinded, rendering it highly subjective. Patient selection criteria are usually not mentioned or are variable in a given series. Diagnostic algorithms to differentiate patients with different types of PVD are rarely used.<sup>121</sup> Most studies do not distinguish among the various forms of vestibulodynia (eg, PVD1 or PVD2). There is a great degree of variability in the length of follow-up

even in a given series, and follow-up is not always long term. Therefore, determining the rate of recurrence of vestibulodynia after surgery is very difficult to assess. Given this complexity, Tommola et al<sup>120</sup> conducted a systematic review of the success rates and complication rates of the several variations of this procedure and concluded: “There is no straightforward recommendation of the best technique. Certainly the surgeon’s experience plays a critical role. As with all surgeries, the procedure should be extensive enough to remove all painful areas but also to avoid unnecessary risks” (p. 1393). As with all surgeries, patients need to be informed of the possible complications of vestibulectomy. Complications are infrequent; as such, their risk should not be overemphasized. They can include bleeding, infection, increased pain, hematoma, wound dehiscence, scar tissue formation, and Bartholin cyst formation.<sup>121</sup>

With these caveats in mind, overall results have demonstrated that surgical management of PVD results in success rates of 60% to 90%,<sup>122</sup> with some studies indicating that women with PVD1 have lower success rates than those with PVD2 (eg, Bergeron et al,<sup>69</sup> Bohm-Starke-Rylander<sup>123</sup>) although this latter finding is preliminary. Many have questioned why surgery is often used as a “last resort,” that is, only after other “less invasive” (ie, conservative) treatment options have not yielded successful outcomes. This paradox can be illustrated by the findings of a study published by Tommola et al<sup>120</sup> in which 66 women diagnosed with severe PVD were followed long term from the time of diagnosis until after successful treatment. Thirty-nine women did not respond to conservative treatment and received posterior vestibulectomies, whereas 27 were managed conservatively with medication. Overall, dyspareunia decreased significantly in the two groups, with 66.7% of women in the surgery group reporting improvement in dyspareunia and 78.1% in the conservative treatment group reporting improvement in dyspareunia. Long-term sexual well-being did not differ significantly between the two groups, and 89% of women in the two groups were satisfied with their overall treatment. This finding suggests that conservative treatment might be preferred as first-line treatment to avoid the inconveniences and long recovery period of the vestibulectomy. We recommend vestibulectomy as a management option for PVD once other less invasive treatment options have been attempted (for most cases; grade B).

## CONCLUSIONS

A comprehensive assessment is needed to understand the pain experience of women presenting with vulvodynia. In addition, treatment typically progresses from less invasive to more invasive, and several treatment options are worth pursuing.

**Corresponding Author:** Andrew T. Goldstein, Center for Vulvovaginal Disorders, 3 Washington Circle NW, Suite 205, Washington, DC 20037, USA; E-mail: [obstetrics@yahoo.com](mailto:obstetrics@yahoo.com)

**Conflict of Interest:** Andrew T. Goldstein has received research funding from Bayer and Palatin and is on the medical advisory

boards for Strategic Sciences and Technologies and Emotional Brain. The other authors report no conflicts of interest.

**Funding:** None.

## STATEMENT OF AUTHORSHIP

### Category 1

- (a) **Conception and Design**  
Andrew T. Goldstein; Caroline F. Pukall
- (b) **Acquisition of Data**  
Not applicable
- (c) **Analysis and Interpretation of Data**  
Not applicable

### Category 2

- (a) **Drafting the Article**  
Andrew T. Goldstein; Caroline F. Pukall; Candace Brown; Sophie Bergeron; Amy Stein; Susan Kellogg-Spadt
- (b) **Revising It for Intellectual Content**  
Andrew T. Goldstein; Caroline F. Pukall; Candace Brown; Sophie Bergeron

### Category 3

- (a) **Final Approval of the Completed Article**  
Andrew T. Goldstein; Caroline F. Pukall; Candace Brown; Sophie Bergeron

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