

Genito-Pelvic Pain/Penetration Disorder (GPPPD): An Overview of Current Terminology, Etiology, and Treatment

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ABSTRACT

Genito-Pelvic Pain/Penetration Disorder (GPPPD) is a relatively new diagnostic category of female sexual dysfunction, which was introduced during the release of the DSM-5 in 2013. GPPPD reflects the combination of two previous categories of female sexual dysfunction, dyspareunia and vaginismus, into one entity. As such, there is confusion surrounding the proper terminology and diagnostic criteria used when evaluating female sexual or genital pain. This review article attempts to clarify the terminologies used within the medical and scientific community, and provides an overview of current views on etiology and treatment. The likely biological antecedents to genital pain are an exaggerated and prolonged inflammatory response in the vestibular mucosa causing neuroproliferation, and leading to eventual hyperalgesia, allodynia, and pelvic muscle tension in the genital region. These processes interact with psychosocial factors to produce chronic pain. Treatment includes education, CBT, pelvic floor physiotherapy, medical interventions, and surgical interventions, though sexual function may be optimized through a multifaceted approach.

RÉSUMÉ

La Genito-Pelvic Pain/Penetration Disorder (GPPPD) est une catégorie diagnostique relativement récente de la dysfonction sexuelle féminine, qui a été introduite dans le DSM-5 en 2013. La GPPPD reflète la combinaison de deux catégories précédentes de dysfonctionnement sexuel féminin, la dyspareunie et le vaginisme, en une entité. En tant que tel, il existe une confusion entourant la terminologie appropriée et les critères de diagnostic utilisés lors de l'évaluation de la douleur sexuelle ou génitale féminine. Cet article de revue tente de clarifier les terminologies utilisées dans la communauté médicale et scientifique et donne un aperçu des points de vue actuels sur l'étiologie et le traitement. Les antécédents biologiques probables à la douleur génitale sont une réponse inflammatoire exagérée et prolongée dans la muqueuse vestibulaire entraînant une neuroprolifération, et conduisant à une éventuelle hyperalgésie, allodynie et tension musculaire pelvienne dans la région génitale. Ces processus interagissent avec des facteurs psychosociaux pour produire une douleur chronique. Le traitement comprend l'éducation, la TCC, la physiothérapie du plancher pelvien, les interventions médicales et les interventions chirurgicales, bien que la fonction sexuelle puisse être optimisée par une approche multidimensionnelle.

For several years researchers and clinicians have struggled with how to best categorize the various forms of female sexual pain, due in large part to significant overlap in symptomatology and treatment [1]. In 2013, a new diagnostic category of sexual dysfunction was established in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), known as Genito-Pelvic Pain/Penetration Disorder, or GPPPD. This disorder encompasses two previously separate disorders, dyspareunia and vaginismus, into one single diagnostic category defined according to the DSM-5 by persistent or recurrent difficulties in the following criteria:

- Vaginal penetration during intercourse;

- Marked vulvovaginal or pelvic pain during vaginal intercourse or penetration attempts;
- Marked fear or anxiety about vulvovaginal or pelvic pain in anticipation of, during, or as a result of vaginal penetration; and
- Marked tensing or tightening of the pelvic floor muscles during attempted vaginal penetration [2].

Any one of the above criteria must be met for a diagnosis of GPPPD, with at least six months duration and the presence of clinically significant distress. The dysfunction may be lifelong (since the individual became sexually active) or acquired, and is classified as mild, moderate, or severe depending on the extent

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of functional impairment [2,3]. While persons with GPPPD may have a broad range of clinical presentations, the defining feature of the disorder is pain or fear of pain upon sexual genital contact or vaginal penetration. Penetration may refer to entry of a penis, but it can also refer to any other object, making tampon insertion or gynecological exams difficult or impossible [2,3].

In contrast, vulvodynia is a closely related and overlapping term used to describe chronic pain in the vulvar region of at least 3 months duration. It may be generalized or localized to a specific area, and provoked by contact or unprovoked (i.e., spontaneous) [4,5]. Vulvodynia is often associated with GPPPD and sexual pain, though not all cases of GPPPD are necessarily caused by vulvodynia [3]. Vulvodynia is not itself classified as a sexual dysfunction, but is a term used to describe a type of chronic genital pain that is present with or without sexual contact [5]. Table 1 summarizes correct terminology between the two conditions.

There are two main subtypes of vulvodynia: provoked vestibulodynia (PVD), characterized by localized provoked pain at the vaginal vestibule (introitus), and generalized vulvodynia (GVD) characterized by unprovoked, diffuse burning pain throughout the entire vulva [4,5]. PVD is thought to be the most common cause of introital dyspareunia, affecting up to 8% of reproductive age women [6,7]. Recent estimates suggest that 17-19% of American women experience coital pain, though epidemiological data can be difficult to interpret as many women may not discuss these symptoms with their physicians due to fear of embarrassment or stigmatization [3,8].

While dyspareunia and vaginismus were both previously classified as sexual pain disorders in the DSM-IV, they were differentiated by their main clinical features. Dyspareunia was characterized primarily by genital pain during intercourse/penetration,

which could be either introital (at the vaginal entrance), deep (deep in the vagina or pelvis), or both [3]. In contrast, vaginismus was characterized by involuntary vaginal muscle spasms which were strong enough to interfere with or prevent intercourse/penetration [3,9].

In clinical practice, however, the disorders were often comorbid or “difficult or nearly impossible” to differentiate: the expectation or fear of genital pain in dyspareunia, for example, may cause involuntary pelvic muscle contraction making intercourse difficult, just as involuntary pelvic muscle contraction in vaginismus may cause genital pain if penetration is attempted [9,10]. Furthermore, vaginal muscle spasm, the defining feature of vaginismus, was not found to be a valid or reliable diagnostic criterion when tested empirically [1,9]. Many researchers felt diagnostic accuracy would be improved through combining both disorders into one unified category. Conversely, some argue that the scope of GPPPD is overly broad and complicates rather than simplifies clinical diagnosis for most practitioners [3,10].

This complication becomes evident when one considers that both vulvodynia and GPPPD are by definition idiopathic, and thus are disorders of exclusion if no medical cause is found [3,5,7]. As specified in the DSM-5 diagnostic criteria, the sexual pain felt in GPPPD cannot be better explained by a medical condition [2]. Similarly, the 2015 Consensus Terminology of Persistent Vulvar Pain and Vulvodynia indicates that vulvodynia must have no clear identifiable cause, otherwise the pain is categorized as persistent vulvar pain [4,5]. Thus, a thorough medical history and exam are essential to rule out potential differential diagnoses that may better explain the woman's pain. In these cases, the treatment of sexual or genital pain would be connected to the management and treatment of her medical diagnosis. However, if the medical cause is successfully treated and the pain has not resolved, a diagnosis of vulvodynia or GPPPD is

Table 1. Correct terminology of sexual/genital pain conditions.

GPPPD	Describes recurrent difficulty/pain on sexual intercourse or penetration attempts, and is classified as a female sexual dysfunction in the DSM-5. May or may not be caused by vulvodynia.
Vulvodynia	Describes idiopathic chronic genital pain localized to the vulva that is present with or without sexual contact. Not classified as a female sexual dysfunction, but can cause or contribute to female sexual dysfunction.



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Table 2. Medical conditions associated with/causative of dyspareunia [4,5,19].

Infectious
<ul style="list-style-type: none"> • Recurrent vulvovaginal candidiasis • Sexually transmitted infection (e.g. herpes) • Pelvic inflammatory disease
Inflammatory/Dermatologic
<ul style="list-style-type: none"> • Lichen sclerosus • Lichen planus • Vulvar granuloma fissuratum • Skin allergy (e.g. semen)
Neoplastic
<ul style="list-style-type: none"> • Paget disease • Vulvar interepithelial neoplasm • Pelvic neoplasms (cervical, uterine, ovarian, colon)
Neurologic
<ul style="list-style-type: none"> • Postherpetic neuralgia • Nerve compression or injury (e.g. pudendal nerve, genitofemoral nerve) • Neuroma
Trauma
<ul style="list-style-type: none"> • Female genital cutting • Obstetrical tears / episiotomy scars
Iatrogenic
<ul style="list-style-type: none"> • Post-operative • Chemotherapy, radiation
Hormonal
<ul style="list-style-type: none"> • Vulvovaginal atrophy secondary to decreased sex steroids secondary to: menopause, lactational amenorrhea, anorexia, hyperprolactinemia, oophorectomy
Structural
<ul style="list-style-type: none"> • Endometriosis • Leiomyoma • Ovarian mass • Pelvic adhesions • Congenital abnormalities of the hymen (imperforate hymen, septate hymen) • Vaginal agenesis

appropriate [4]. See Table 2 for possible medical causes of dyspareunia which should be ruled out or treated before considering a diagnosis of GPPPD.

ETIOLOGY

The etiology of GPPPD is multifactorial and complex, in that biological, psychological and relational factors interact to perpetuate and maintain a woman's pain response. What may initially be an adaptive nociceptive response resulting from peripheral tissue damage may gradually shift to a neuropathic and/or inflammatory pain in the absence of acute injury. It is this maladaptive pain that is harmful to sexual functioning, especially with increasing involvement of the central nervous system in pain sensitization [3,11]. Thus, GPPPD should be evaluated from a biopsychosocial perspective, and should never be viewed as a purely psychogenic problem [3,4].

Biological

Mast cell activation signifies the presence of inflammation and has been found in response to mechanical trauma or mucosal damage caused by infections, inadequate lubrication during

sexual intercourse, chemical irritation (from soaps, douches, etc.), and allergic reactions [3]. Interestingly, studies evaluating vulvar histology in patients with vulvodynia have found increased inflammatory cell infiltrate in painful regions of the vulvar vestibule, and increased mast cell presence in areas of vestibular pain [4,12].

Prolonged tissue damage can lead to mast cell hyperactivation, resulting in over-production of inflammatory molecules and neurotrophins [3]. One such neurotrophin, Nerve Growth Factor (NGF), both has pro-inflammatory roles and induces the proliferation of peripheral nociceptors [11]. Over time, the concentration of mast cells in the inflamed tissue decreases, but there is a corresponding increase in nerve endings resulting in increased sensitivity to painful stimuli (known as hyperalgesia) and causing ordinarily non-painful stimuli to become painful (known as allodynia) [3,11]. Hyperalgesia and allodynia are characteristic of neuropathic pain. Painful stimuli can then cause defensive muscle contraction and eventual hyperactivity and dysfunction [3,4].

Such a mechanism has been proposed in vulvodynia and GPPPD, in which chronic inflammation of the vulvar epithelium (or an abnormal inflammatory response) leads to mast cell hyperactivation, sensitization and proliferation of pain nerve fibres in the area, and resultant pain and hypertonicity of the pelvic floor [3]. In fact, biopsies from the posterior vestibule in vestibulodynia patients confirm the presence of an increased number of free nerve endings when compared to healthy control subjects [13,14]. While nociceptor proliferation has not been found in vulvar tissue samples of patients with generalized vulvodynia, this may be due to a preponderance of research focusing on PVD, and much less on GVD [3].

Some studies suggest that there could be a genetic propensity to develop chronic inflammatory conditions, caused by an abnormal and overactive inflammatory response with a reduced ability to terminate such inflammation. For example, women with vulvodynia are significantly more likely to report other comorbid chronic medical conditions, such as interstitial cystitis, irritable bowel syndrome, and fibromyalgia than those in the general population [3,4]. Women with vulvodynia also seem to react more frequently than control subjects to Candida patch tests, possibly indicating a contact hypersensitivity to the infection [15]. However, more research must be done before suggesting a strong genetic link.

Finally, there is some evidence to suggest that prolonged use of oral combined hormonal contraceptive pills (CHCs) may increase the relative risk of developing PVD due to the resulting decrease in circulating estrogen and testosterone [4,7,10]. This can cause morphologic changes to the vulva, decreasing the size of the clitoris, thickness of the labia and diameter of the introitus, and ultimately rendering the vestibular mucosa more vulnerable to mechanical stress [4,16]. However, CHC use is common in North America, and most women do not go on to develop vulvodynia [4].

Psychosocial

As unwanted pain dampens the sexual response, there may be a progressive withdrawing from sexual interactions [9]. Several controlled studies have shown that women with vulvar pain have a higher incidence of depressive symptoms than controls, and report an increased loss of working days [3,4]. Catastrophizing pain, fear of pain, hypervigilance to pain, low self-efficacy, avoidance, anxiety, and depression may all intensify the experience of pain and perpetuate sexual dysfunction. Conversely, higher self-efficacy (i.e., beliefs that one can successfully manage the pain) may lead to reductions in pain intensity during penetration attempts [17]. Furthermore, pain (and anticipation of pain) reflexively inhibits both mental and physical sexual arousal, thus decreasing vaginal lubrication, vulvar congestion, pelvic muscle relaxation, and sexual pleasure [3]. This makes the vaginal mucosa more susceptible to micro-abrasions and tears, resulting in additional genital pain and inflammation upon penetration attempts.

Women with partners who respond to their sexual pain in a way that facilitates adaptive coping, as opposed to paying excessive attention to the problem or demonstrating hostility, have been found to have higher levels of sexual satisfaction, relationship satisfaction, and lower ratings of pain [4,18]. Thus, the way a partner responds to chronic pain can help or harm the ability to manage painful stimuli. It should be noted here that sexual pain disorders can affect women in same-sex relationships as well, so care should be taken not to assume that sexual pain during penetration is limited to penile-vaginal intercourse within traditional heterosexual relationships.

An understanding of the woman's background, including cultural context, past relationships, sexual education and knowledge of personal anatomy and physiology, may also be important in guiding future discussions of possible cognitions, emotions or behaviours that may be contributing to her pain

[9,19]. This is especially relevant if there is significant shame or feelings of inadequacy surrounding sexual functioning, or if there is a history of past sexual or physical abuse.

Unremitting sexual and genital pain can be incredibly disheartening for many women, especially if they feel invalidated by their health care team, by their partners, or by society [4,9]. One study found that fewer than 50% of all women who met criteria for vulvodynia sought treatment, reflecting the apprehension of sufferers to speak about their pain [20]. Additionally, many physicians lack the knowledge to manage sexual pain disorders.

TREATMENT

The aim of treatment is two-fold: (1) to reduce sexual and genital pain, and (2) to restore or improve sexual function [8]. As clinical presentations of GPPPD and vulvodynia can vary widely, treatment should be client-centered and tailored to the unique characteristics of the specific individual undergoing treatment. However, a general guideline to progress from least to most invasive treatment options is usually followed [7,8,19]. As mentioned previously, possible medical causes of pain should be assessed and treated first and foremost, before attempting treatment of idiopathic sexual or genital pain [3].

Non-Medical Approach

Education about vulvar self-care, including avoidance of douches, possible irritants, and allergens, is an important first step for practitioners [8]. Knowledge of genital anatomy and the female sexual response cycle may also be beneficial to facilitate greater understanding of what to expect from sexual encounters and to reduce anxiety [9].

Psychological intervention, often in the form of CBT, aims to explore a woman's thoughts, emotions, behaviours and relationship dynamics associated with the experience of her sexual pain. Thus, maladaptive or unhelpful cognitions that may be perpetuating the physical experience of pain or feelings of fear and anxiety can be identified and replaced with more helpful thoughts [8,19]. This may be undertaken individually, as a couple, or in a group. Research supports the effectiveness of individual CBT, with improvements in pain and sexual function maintained at one year when compared to individual supportive therapy [21]. Similar positive results were found in couple- and group-based CBT [8,19]. One study demonstrated that patients treated with group-CBT had similar self-reported ratings of coital pain at a 2.5-year follow-up when compared to

patients who underwent surgery [22].

Pelvic floor physical therapy, aims to reduce elevated tone or tension in the pelvic floor muscles that are contributing to the experience of sexual pain and making intercourse painful or difficult. This is done through increased awareness of pelvic muscles, improving relaxation techniques, normalizing tone, and providing stretching stimuli at the introitus to gradually reduce anxiety surrounding penetration [8,19]. The approach is often multimodal, and encompasses techniques such as electromyographic biofeedback (EMG), electrical stimulation, manual tissue manipulation, stretching/strengthening exercises, and the use of dilators or accommodators [8-10]. A retrospective study evaluating a pelvic floor physical therapy program found that after an average of 7 sessions, 51.4% of women with PVD had complete or great improvement and 20.0% has moderate improvement in pain at follow-up, with average coital pain intensity ratings decreasing from 8.2 to 3.9 after treatment [23].

As sexual pain disorders involve the interplay between many different though related factors in their onset and progression, an interdisciplinary approach that utilizes a multimodal treatment plan may work best in improving pain scores and sexual function [8,19]. In encompassing the biomedical, cognitive, affective, and relational components of treatment, the unique circumstance of each patient is taken into account and may provide a sense of validation and support. Thus, an integrated approach to treatment will likely produce better outcomes than a single modality alone.

Medical Approach

Anti-nociceptive agents are primarily used when neurogenic pain is suspected [8]. Local anesthetics such as topical lidocaine attempt to block peripheral nerve transmission by acting on sodium channels in nociceptors. However, they have been found to be minimally efficacious, with one study demonstrating only a 20% improvement in pain scores which was not significantly different from placebo [24]. Capsaicin, conversely, decreased pain with intercourse by 95% in one study, though the residual burning sensation was not tolerable as a side effect for many women [8,25]. Botulinum Toxin Type A (Botox) acts at nociceptors to cause local muscle paralysis of 3-6 month duration, making it an appropriate choice for women who have difficulties with pelvic floor hyperactivity causing pain. Several small studies have demonstrated efficacy in improving sexual pain, though larger RCTs should confirm these results before recom-

mendation as a first-line treatment [8,26,27].

Anti-inflammatory agents such as corticosteroids have had only minimal efficacy in treating genital pain, despite increased IL- β (typically decreased by corticosteroids) being found in the hymenal tissues of women with PVD [8,19]. Cromolyn cream (a mast cell stabilizer), enoxaparin (a low molecular weight heparin), and a skin cream containing lysate of fetal fibroblasts (with anti-inflammatory cytokines) have all undergone RCTs to evaluate the efficacy of possible anti-inflammatory action, with various success [28-30].

As CHCs may contribute to hormonally associated PVD in some women, there is evidence to suggest that topical estradiol and testosterone gels may improve pain scores significantly in such cases [8,10-19]. Vestibular pain scores decreased from 7.5 to 2.0 in a 50-woman, non-placebo-controlled retrospective study for those who developed vulvodynia secondary to CHCs, with treatment using topical 0.03% estradiol and 0.01% testosterone and discontinuation of CHC use [31]. However, more research is needed.

A literature review evaluating the effectiveness of tricyclic antidepressants suggest that they should not be used in the treatment of genital pain due to lack of sufficient evidence [32]. However, a recent small open-label trial of SNRI seemed to reduce pain severity, coital pain, and depression symptoms, though the study was small and non-blinded [33]. Thus, more research into the use of antidepressants as a treatment option is warranted.

Surgical Approach

Vulvar vestibulectomy, or the complete removal of the vestibular mucosa, is a well-established treatment for PVD associated with neuroproliferation [8,19]. While this is the most invasive approach to treatment, the success rates are high, with at least partial relief of sexual pain in 88% of patients and significant relief in 78.5% of patients according to a meta-analysis of 33 previous studies [34]. Of course, as with all invasive procedures, there is a risk of complications such as bleeding, infection, and worsening of pain. However, complications are infrequent, and surgery may prove to be extremely beneficial in managing vestibular pain in women who are resistant to less invasive treatment options [8,19].

CONCLUSION

Recurrent genital and sexual pain is a highly distressing condition encompassed by the diagnoses of vulvodynia and GPPPD. The etiology of sexual pain disorders is complex and involves many interrelated factors that are often difficult to separate within the clinical setting. Nevertheless, effective treatment options are available, generally progressing from least to most invasive. Given the medical, psychological, relational, and cultural connections to the experience of vulvar and sexual pain, a multidisciplinary approach is optimal to achieve the most effective impact on chronic pain symptoms, sexual functioning, relational satisfaction and quality of life. More research in the form of randomized controlled trials is needed to elucidate which medical treatments are effective in long term genital and sexual pain reduction.

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