

Vulvar Vestibulitis Syndrome: A Clinical Approach

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Abstract

Vulvar Vestibulitis Syndrome (VVS) is a heterogeneous, multisystemic, and multifactorial disease, and is one of the leading causes of dyspareunia in fertile women. As a multisystemic disease, it involves the mucous structure of the vulvar vestibule and the immune, muscular, vascular, and nervous systems, and involves pain fibers and centers. As a multifactorial disease, its etiology is complex and multiple, involving biological, psychosexual, and relational factors. The progression of the disease, and the impact of an often lengthy delay between the onset of symptoms and a correct diagnosis are discussed. Moreover, despite documented improvements from available treatments, VVS becomes a chronic disease, unless diagnosis is early, and an integrated, pathophysiologically-oriented treatment is offered in an experienced center. Health care providers would therefore benefit from approaching the condition within a management framework focused on the woman's chronic pain, the impact on the couple's relationship, and any psychological sequelae from the condition.

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Background

Vulvar Vestibulitis Syndrome (VVS) is a heterogeneous, multisystemic and multi-factorial disease, and is one of the leading causes of dyspareunia in women of fertile age (Baggish & Miklos, 1995; Bergeron, Binik, Khalife, & Pagidas, 1997; Friedrich, 1987; Graziottin, 2001). VVS has been described as a clinical disease with three symptoms and signs: 1) severe pain on vestibular touch or attempted vaginal entry; 2) tenderness when pressure is localized within the vestibule; and 3) physical findings confined to vestibular erythema of various degrees (Friedrich, 1987). Revised criteria have been proposed (Bergeron, Khalife, Pagidas, Meana, Amsel, & Binik, 2001), but the diagnosis is still based on Friedrich's criteria. VVS is one aspect of "vulvodynia", a clinical condition well described by the International Society for the Study of Vulvovaginal Diseases. Understanding the pathophysiology involved in the diagnosis of VVS, so that optimal treatment recommendations may follow, is currently a challenge for clinicians and researchers in the field of female sexual medicine, and is the topic of a forthcoming article from these authors. The focus of this paper is on the optimal management of chronic pain in women with VVS, psychological sequelae women may experience, and on relationship factors resulting from the condition. These aspects are critical to address if there is to be a shift from pain to pleasure; in other words, the ideal endpoint in our intervention is the re-acquisition of a satisfying sexual experience for the woman and her partner. A brief summary of key pathophysiological concepts may help to design an optimal medical and psychosexual intervention in a step-care multidimensional model.

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The Natural History of VVS

The concept of “Natural History” is basic in understanding the spontaneous evolution of a disease, and to design the step-care rationale of a medical and psychosexual intervention. Natural history highlights a number of key concepts that apply well to VVS as well, as illustrated in Figure 1: (1) Firstly, the number and type of factors that concur to a clinical picture changes and increases over time, particularly in chronic diseases which involve multiple biological systems [e.g., nervous (including the pain system, a key protagonist in VVS), vascular, immune, and muscular]. (2) Secondly, the impact the disease has on the affected person increases over time, with complex adaptation of and changes in his/her psychological well-being and coping style, as well as in couple and family dynamics. This is true also for diseases with an initial strong biological base, like VVS, particularly when burning pain becomes a hallmark of the disease. (3) Thirdly, predisposing, precipitating, and maintaining factors in VVS should be recognized and addressed. Metaphorically speaking, the natural history of a disease is like a movie, where the moment of the diagnosis is just one segment of the story. The protagonists of that scene may be very different from those present at the beginning of the story. Moreover, the possibility of changing the end of the story is greater at the beginning and decreases progressively over time, particularly if one hopes for a happy ending. This holds strongly true in VVS, where the shift from nociceptive pain (a condition in which ongoing acute tissue damage leads the organism to withhold and defend itself) to neuropathic pain (a condition wherein pain is generated within the pain fibers and centers themselves) is not only the hallmark of the disease but also its most challenging feature (Figure 2; Graziottin & Vincenti, 2002). The

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proliferation of introital nociceptive fibers is well documented in VVS (Bohm-Starke, Hilliges, Falconer, & Rylander, 1999; Bohm-Starke, Hilliges, Blomgren, Falconer, & Rylander, 2001; Bohm-Starke, Hilliges, Brodda-Jansen, Rylander, & Torebjork, 2001). The concept of “neuropathic pain” is gaining increasing attention in the scientific literature (Baron, Levine, & Fields, 1999; Baron, Schattschneider, Binder, Siebrecht, & Wasner, 2002; Bonica, 1990). The transition from the nociceptive to neuropathic pain is key in VVS as it underlies the shift from a sexual pain disorder – where intercourse elicits and provokes pain - to a progressively pure pain disorder, which is self-maintained in spite of the avoidance of any further coital intimacy. Some women with chronic VVS report distress over non-coital activity such as kissing or hugging their partner, or even upon having an erotic dream or watching an erotic movie, as even the mild genital arousal (without any direct contact) immediately elicits a worsening of the VVS pain. (4) Finally, the time delay from disease onset to the moment of a clinical diagnosis is critical (as shown in Figure 1), as this may clarify which factors are implicated, which are still reversible, how to choose between conservative vs invasive and surgical treatments, and overall how the prognosis may vary.

As a multifactorial and multisystemic disease, with a potentially chronic course, VVS requires attention to the biological, psychosexual, and relational co-factors in a clinically oriented way. Complex problems require complex solutions, and in terms of the tendency to search for “the” treatment, VVS is one condition in which this key conceptual mistake is common practice. There is no simple treatment that may address the complexity of the etiological factors in VVS and of their variable impact on the women’s profile and on the couple’s dynamics over time. Moreover, all proposed treatments are designed to reduce and hopefully eliminate pain. However,

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in a sexual pain disorder, this would be an incomplete outcome. A true therapeutic success takes place when the woman regains a satisfying sexual life.

The clinical diagnosis of VVS

A tentative diagnosis of VVS should be considered when a woman reports superficial dyspareunia with introital contact, and a clinical examination reveals the three hallmark symptoms described by Friedrich. From the perspective of the practicing physician who most frequently encounters women presenting with such complaints, a focused clinical assessment helps to ensure an accurate diagnosis of VVS, and helps to focus optimal management. We summarize the components of a thorough clinical assessment in nine categories that include both objective testing with a physical examination by the physician, as well as subjective assessment of the woman's self-reported experience.

First, an accurate psychosexual history, focusing on the occurrence of any sexual dysfunction present before the onset of VVS, must be assessed. The woman's current sexual practices, and the co-existence of any sexual dysfunction, delineating life-long versus acquired desire, arousal, orgasmic, and satisfaction difficulties, besides dyspareunia must be evaluated. If there are signs of a general defensive posture (defined as a dramatic increase in muscle tension, with avoidance of any genital contact, including avoidance of the examiner's hand), and a history of lifelong dyspareunia, this may point to a primary condition of vaginismus, co-occurring with the VVS (Van der Velde, Laan, & Everaerd, 2001). Second, a detailed medical history must be undertaken that includes assessment of food and medication intake. In particular, any food intolerance, allergy, current hormonal treatment (e.g., oral contraceptive pill, hormone replacement therapy), and all previous systemic and

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genital treatments must be assessed and recorded. Third, the physician should inquire as to previous vaginal infections or sexually transmitted diseases, such as candida, gardnerella, Human Papilloma Virus (HPV), and herpes. The status of current vaginal bacterial culture and infection must be tested with a vaginal swab and subsequent cultures, especially if an ongoing infection is suspected. Moving to the more qualitative aspects of the assessment, the fourth step involves determining the woman's perception of the characteristics and duration of symptoms. This might involve taking a developmental perspective (i.e., the natural history approach) to trace the onset of VVS symptoms. Fifth, a very careful physical examination should be recorded. Vaginal pH should be tested objectively with a vaginal stick for 10 - 15 seconds during the gynecological examination (Caillouette, Sharp, Zimmerman, & Roy, 1997). Step six involves asking three basic questions about the quality of the pain: "Where does it hurt?", "When does it hurt?", and "What are the associated symptoms you experience?". These three questions have been suggested to reliably indicate the relevant biological etiology of dyspareunia in women (Meana, Binik, Khalife, & Cohen, 1997) and should guide the objective clinical recording of the next step. The seventh step is the key feature of the examination: the making of an accurate "pain map" - the precise recording of any point in the external genitalia, mid- and deep vagina where pain can be objectively elicited, in parallel with the questioning (Graziottin, 2001, Graziottin, Nicolosi, & Caliarì, 2001c). An accurate gynecological examination may reproduce exactly the pain site and characteristics the woman experiences in 90% of cases (Bergeron et al., 2001). This is done through a careful gynecological examination, paying attention to any increase in pain perception in the vulvar and vestibular areas, at the mid-vagina, and at deep insertion. The precise location of pain, it's onset, and it's characteristics have proven

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to be the strongest predictors of its organicity (Meana et al., 1997). The gynecological examination should also pay attention to the presence of other complicating factors, such as defensive levator ani contraction that over time may become a cofactor of pain, leading to levator ani myalgia. This reflex contraction may be present from the onset of sexual activity (i.e., lifelong), where vaginismus is present, or may be acquired in response to pain, as an automatic defensive measure to prevent further penetration and consequent pain and tissue damage. The progressively intense myalgia that may develop further increases the generation and perception of pain, and consequently prevents penetration. The presence of such factors would necessitate a more comprehensive, rehabilitative treatment, aimed at relaxing the tightened pelvic floor. Next, bilateral quantification of the perception of the pain intensity should be recorded using a Likert scale (from zero - no pain, to ten - worst pain ever). This is done bilaterally because higher pain perception is usually reported on the left side, possibly for postural/antalgic reasons and/or the habit of having a preferred crossed leg, which causes different tension in the two halves of the levator ani. Other medical conditions that could be objectively diagnosed and that could be a cofactor of pain should as well be recorded (e.g., painful episiorraphy, dystrophias, associated clitoralgia, etc.). Finally, as sexual activity typically involves a partner, the status and quality of the relationship, focusing on their affective, sexual, and interpersonal functioning, should be assessed. Given that aspects of a partner's functioning have been shown to affect sexual functioning of the woman (e.g., Dennerstein, Lehert, Burger, Garamszegi, & Dudley, 2000; Kaplan, 1974), the presence of sexual and/or genital symptoms of the partner should be recorded as well.

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Prognosis

Few data are published on the prognosis of VVS in women following treatment. Even less is known about putative characteristics of the woman at the time of assessment that might suggest a particular prognosis. We would suggest an algorithm based on a tentative clinical categorization to guide prognosis. Type one could be described as “Low risk VVS patients, with good prognosis”. Aspects of their detailed clinical assessment that might suggest such a prognosis would include: 1) VVS duration less than one year; 2) normal systemic pain threshold; 3) no history of invasive treatments; 4) no difficulties with sexuality before the VVS symptoms; 5) demonstrable self-efficacy and coping strategies; and 6) a positive relationship with a supportive partner. Type two could be described as “High risk VVS patients, with questionable prognosis”. Aspects of their clinical assessment that might signal such a prognosis would include: 1) VVS duration of more than one year; 2) chronic candida and/or candida treatment resistant; 3) experienced vulvar or vestibular HPV laser treatment; 4) hyperalgesia (local and systemic); 5) sexual difficulties present before the onset of VVS; 6) endorsement of depressive symptoms; 7) endorsement of anxiety symptoms, which might include fear of sexual intimacy or avoidant behaviour; and 8) being single or in a troubled relationship. A third type of prognostic categorization could be described as “High risk VVS patients, deserving systemic and local analgesic treatment, in addition to psychosexual support. This classification would be considered when there is: 1) pain persisting after electroanalgesia, electromyographic biofeedback, and/or vestibulectomy (Graziottin & Vincenti, 2002); 2) burning pain becoming independent from intercourse; and 3) high personal and/or couple distress.

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Treatment guidelines

Given the complex etiological and pathophysiological processes involved in VVS, treatment requires a therapeutic approach that combines attention to the biological as well as psychosexual domains (Figure 3).

a) Medical approach

With respect to biological precipitants, treatment of an associated genital disease or infection, muscle tension of the pelvic floor, and pain, must take place. If there is a precipitating infectious disease, such as candida or gardnerella (Faro, 1996; Horowitz, 1991; Paavonen, 1995), or less frequently HPV or herpes, the following treatments are suggested: (1) when present, chronic candida is to be treated with itroconazole, 200 mg/orally/day for three days (or fluconazole 100 mg/oral/day for two days) every 2 weeks for three months, then once/month for another three months. The partner should also be treated for the first month. This treatment is aimed at reducing the recurrent episodes of candida that might perpetuate the vaginitis and the mast-cell hyperactivation. In a review of the cases seen in our center, a history of chronic vaginal candida infections were reported in 58.1%, and in 29.0% this was confirmed upon presentation to our centre (Graziottin, et al., 2001a) . According to some authors (Mariani, 2002) patients with a positive culture for candida and symptoms flaring with menses are thought to be better categorized as “cyclic vulvitis” (McKay 1992) or “atypical “ candidiasis and are thus removed from the classification. However, when recurrent candida is associated with the specific triad of VVS features, the condition should be addressed in parallel with VVS treatment. Recurrent Gardnerella or Haemophilus infection (Paavonen, 1995), reported in 33.9% of our patients (Graziottin et al., 2001a), is usually associated with a vaginal pH of 5. Lowering of the pH may be obtained with vaginal tablets of boric

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acid (300mg), a galenic preparation, once/day for 10 days every month (following menstruation). Topical estrogen might be prescribed if the patient has a persisting amenorrhea with vaginal dryness as an associated symptom; or with long acting polymeric acid gel, delivering H⁺ (and thus lowering the pH) twice a week. However, topical treatments should be avoided in the acute phase of the disease as a vaginal/vestibular hyper-reactivity to almost all topical compounds is usually reported. The reactive myalgic tension of the pelvic floor should be addressed by teaching: 1) how to voluntarily relax the pelvic floor muscles; 2) how to self-perform an accurate stretching of the pelvic floor muscles (Graziottin, 2001) in addition to self-massage, five minutes twice a day with a medicated oil (Saint John's wart or hyperico oil), and 3) how to do a circular massage at the tender points on the painful muscle (mid vagina, at the insertion of the levator ani on the ischiatic spine). These simple and effective techniques are especially beneficial for patients who are unable to travel long distances for weekly physiotherapy or electromyographic biofeedback treatment (Graziottin, 2001). Self-massage and stretching are "home made", cost-free, and empowering for the woman to feel progressively more aware of her defensive contraction and in control of at least of one component of her pain. All our patients are encouraged to do their massage on a regular basis. If the partner is present and the woman is accepting, the partner can be taught to recognize the different levels of contraction and relaxation and, in the final phase of treatment, to include the gentle relaxing massage of the pelvic floor during foreplay. Physiotherapy treatment, consisting of two sessions of general relaxation and postural changes, and eight sessions of levator ani surface electromyographic biofeedback, with self-insertion of a small single user s-EMG sensor into the vagina (Glazer, Rodke, Swencionis, Hertz, & Young, 1995; McKay, Kaufman, Doctor,

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Berkova, & Glazer, 2001) is also recommended. Treatment of the pain itself is dependent upon the severity, and upon the degree of impairment in daily life. Pain might best be addressed with surface electroanalgesia to modulate residual vestibular pain, when mucosal integrity is maintained (Nappi, Ferdeghini, Abbiati, Vercesi, Farina, & Polatti, 2003). Mood modulation is recommended with low dose SSRI when depressive symptoms are complicating the condition. Systemic oral analgesia is gaining increasing attention, as research indicates a significant lowering of the systemic pain threshold in these unfortunate women (Pukall, Binik, Khalife, Amsel, & Abbott, 2002). Systemic treatment might include: a) tricyclics aimed at modulating the serotonin and epinephrine imbalance associated with persisting pain (Mariani, 2002; McKay, 1993); or b) anticonvulsants, like gabapentin, aimed at raising the threshold for the amount of stimuli needed for nerves to fire, thus raising the central pain threshold (Graziottin & Vincenti, 2002). Presacral anesthetic block of the ganglion impar has recently been proposed as an effective conservative second-line treatment when all previous treatments have failed (Graziottin & Vincenti, 2002). To the best of these authors' knowledge, this technique, proposed by Plancarte and colleagues for the treatment of neuropathic pain in patient with recurrent pelvic cancer (Plancarte, Amescua, & Patt, 1990) has not been reported so far in the clinical literature on VVS. This technique is used by our team when genital pain of VVS is resistant to all the above mentioned treatments, and when the characteristics of pain become unbearable and unremitting day and night, thus preventing all kind of daily activities, and having significant effects on mood and well-being. It requires an experienced and skilled anaesthetist with special training in analgesic treatments. Vestibulectomy has been shown to be an effective treatment for VVS (Bergeron et al., 2001; Schneider, Yaron, Bukovsky, Soffer, & Halperin, 2001;

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Weijmar Schultz, Gianotten, van der Meijden, van de Wiel, Blindeman, Chadha, & Drogendijk, 1996) after the failure of more conservative pain treatments. The rationale is to remove the mucosal tissue with nerve proliferation and hypersensitivity, to restore a more normal perception. However, this surgical approach is discussed by those clinicians who consider that the inadequacy of our knowledge on pathophysiology of VVS shouldn't lead to a kind of surgical impulsivity, particularly when outcome measures are somewhat questionable (Marin, 2001). Moreover, a number of post vestibulectomy patients, with persisting and even worsening pain, are subsequently examined at our center, suggesting that more conservative and systemic treatments to keep pain under control should take place before surgery is considered.

b) Psychosexual approach

The psychosexual domains require a detailed clinical assessment by a physician with some knowledge of psychological processes and how these might interface with medical issues. Following significant reduction in the clinical signs and symptoms, and VVS per se is cured or significantly improved, the second part of treatment is to be initiated – objectively quantified as the re-experience of sexual satisfaction and hopefully of coital pleasure. However, the timing of the psychosexual intervention should be tailored according to the diagnosis: i.e., if a concomitant story of traumatic harassment is reported, or an abusive partner is impacting the woman's coping ability, this deserves attention in parallel with medical treatment. The role of psychosexual factors in contributing to the vulnerability of VVS is increasingly acknowledged (Brotto, Basson & Gehring, 2003; Jantos, & White, 1997; Meana et al., 1997, van Lankveld, Weijenberg, ter Kuille, 1996; Sackett, Gates, Heckman-Stone, Kobus, & Galask, 2001; Graziottin, Nicolosi, & Caliarì 2001b). In our VVS

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series, lifelong low libido was reported in 22.7% of patients, and acquired in 58.1%; the remaining reported non-problematic sex drive; lifelong arousal disorder was acknowledged by 17.7% , whilst acquired arousal disorder was reported in 50.0%, with the remaining still reporting normal mental and genital arousal at least during foreplay. Lifelong dyspareunia was complained of by 29.0% of our VVS patients (well addressing the issue of a likely primary vaginismus as well as concomitant low libido and/or arousal disorders as co-factors); acquired in 61.3%; with the remaining 9.7% reporting a recurrent dyspareunia from the beginning of their sexual life, with periods of remission prior to the current persisting problem. Lifelong orgasmic disorders were reported in 17.7%; acquired in 40.3% (most because of coital pain); whilst 41.9% reported no changes in their orgasmic potential during foreplay (Graziottin, Nicolosi, & Caliarì, 2001b). Sexual harassment was reported by 29.2% of our VVS patients, with penetrative abuse in 6.5% (Graziottin, Nicolosi, & Caliarì, 2001b). Poor arousal may indeed favour introital mechanical microabrasion due to the vaginal dryness concomitant to sexual comorbidity (low libido, often associated with long lasting dyspareunia) and the tightened pelvic floor that squeezes and narrows the introitus.

In parallel with an individual approach, couple treatment should be offered to VVS patients, with the psychodiagnostic and therapeutic approach being carried out by an experienced psychiatrist or psychotherapist with sexological training. Key points of the psychosexual intervention are: a) psychodynamic/interpersonal treatment when lifelong issues are at play (e.g., previous harassment or abuse, poor couple differentiation (Schnarch, 2000), poor coping attitude with a catastrophizing approach to life difficulties and VVS), and/or concomitant depression; b) short psychosexual behavioural therapy when a lifelong vaginismus is diagnosed, and/or

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when erotic illiteracy, sexual inhibition, or poor sexual skills are present in the woman and in the couple; c) clitoral vibrators, a clitoral therapy device, and/or vasoactive drugs may be considered to improve genital arousal when pain has been relieved and sexual intimacy is gradually to be resumed. The psychosexual intervention should be integrated with a tailored pharmacologic management of depression or anxiety when they are diagnosed as significant co-factors in the maintenance of low libido, poor arousal and of a general tendency to sexually avoidant behaviour, because of the persisting fear of pain. The aim of the psychosexual and pharmacologic intervention is to re(gain) a serene and satisfying sexual intimacy after months and, more often, years of a burning pain priming the genital area and the entire genital psychosexual experience.

On the basis of these recommendations, two subgroups of patients can be recognized, with a full spectrum of intermediate characteristics in between. At one end might be women (and couples) who had a disappointing sexual life from the beginning of their sexual experience. In these patients, curing VVS is a preliminary part of a more complex treatment aimed at significantly improving the whole sexual experience. Psychotherapeutic and sexual support is recommended, with a treatment aimed at re-exploring the individual's pleasure capacity, addressing individual and couple foreplay first, with intercourse being re-introduced only in the final sessions. Clitoral vibrators, and lubricants may all prove to be useful in increasing genital arousal and experiencing with women, though the empirical data here are scant. Another type of presentation might be the woman with a full pleasurable orgasmic sexual experience, who had an acquired dyspareunia of a variable intensity before VVS was diagnosed. For these patients the normalization of the vaginal/vestibular area may usually lead to a rapid return to a normal sex life,

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unless the symptom duration has been so long as to impair the relationship and any remaining sexual intimacy.

With respect to psychosexual support of the couple, the very first therapeutic step is to explain to the partner what VVS is from the medical point of view, it's strong biological nature, pain being generated in the affected tissue and not "in her mind" . An accurate and yet simple explanation of the medical basis of VVS may have a profound impact on the partner's attitude, that may shift from variably abusive (after months or years of having being told that this was a psychogenic pain, that everything was fine, and that she was just refusing to have intercourse), to apologizing, understanding and becoming supportive. One may show the partner (with the woman's permission) the pain map, and the objective sites of pain in a non sexual condition, and how to relax the tightened pelvic floor, all of which may have profound effects on the couple dynamics. Explaining the rationale of a complex and gradually effective therapeutic approach helps the couple to give meaning to their long suffering, gives a directions to their coping efforts and a new hope to start from. A specific psychosexual intervention is required if the partner suffers from a male sexual dysfunction that could be present before VVS or which appeared during the course of it. Loss of libido in the male partner and/or avoidance of intercourse for fear of causing to the female partner further pain is a common but usually unaddressed aspect of VVS. The longer the chronicity of VVS, the higher the likelihood of a shared disinvestment from the coital intimacy. After curing pain, the pursuit of pleasure requires a committed therapeutic approach. An often unconsidered etiological factor in the maintenance of pain is resuming coital activity despite a lack of sexual arousal. This is likely the most reliable way of causing

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further microtrauma to the vulnerable vulvar vestibule, re-starting the vicious cycle that maintains chronic coital pain.

Conclusion

VVS is a heterogeneous, multisystemic and multifactorial disease. An accurate clinical diagnosis of different biological, psychosexual and relational factors that may act as either vulnerability sexual traits, precipitating and/or reactive factors, should be carried out to establish the treatment (s) that may better address the etiologic complexity of VVS. Different treatment strategies should be recommended, according to the etiologic factors that come into play, the individual risk profile, and any context-dependent factors (i.e., distance from the referral centre) that may make full treatment adherence difficult. A better understanding of the pathophysiology of the disease is necessary if we are to shift from a pragmatic, symptomatologic approach to a more pathophysiologically-oriented one. On a final note, pain is (almost) never psychogenic and VVS is no exception. Patients should no longer be told “The pain is all in your mind” or “It’s psychogenic”. Providing understanding and respect to the emotional needs of this painful sexual experience is a crucial first step in effective therapeutic alliance.

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Figure Caption

Figure 1. Natural History of VVS with time, showing the presence of different concomitant etiologies: a) predisposing factors (e.g., lifelong female sexual dysfunction (FSD), including vaginismus as well as pain vulnerability and personality characteristics); b) precipitating factors (e.g., recurrent vaginitis, candida); and c) maintaining factors (e.g., lifelong or acquired hypertonic pelvic floor; lifelong or acquired low libido, poor arousal and dyspareunia; acquired shift from nociceptive to neuropathic pain).

Figure 2. Descriptive model outlining the progressive shift from nociceptive to neuropathic pain when the persistence of etiological factors in vulnerability of the pain system leads to chronic pain.

Figure 3. The VVS therapeutic approach combines medical (light gray boxes) and psychosexual (dark gray boxes) approaches.

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