SEXUAL PAIN DISORDERS IN ADOLESCENTS

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INTRODUCTION

The sexual pain disorders included in different editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R 1987; DSM-IV-TR, 2000) are dyspareunia and vaginismus. Both these clinical entities have undergone intense scrutiny and international discussion in the more recent years (Basson et Al 2003; Binik 2005; Graziottin, 2005; Meana et Al, 1997; Pukall et Al, 2005, Reissing et Al, 2003, 2004). The key issues of current controversies will be summarized, to give the reader an updated perspective. At the same time, the focus of this paper will be on the pathophysiology of dyspareunia and vulvar vestibulitis (Friedrich, 1987), a subset of vulvodynia, which is one of the leading causes of sexual pain disorders in adolescents. Special attention will be devoted to current research on predictors of vulvodynia in this younger cohort (Bouchard et Al, 2002, Harlow et Al. 2001, Harlow & Stewart 2003). The aim is to discuss key practical issues relevant for the clinician, working with adolescents, in his/her daily practice.

DEFINITION OF DYSPAREUNIA

Dyspareunia is a comprehensive word, used when intercourse is characterized by pain, of different etiology (Friedrich, 1987; De Lancey et Al, 1993; Glazener, 1997; Graziottin, 2001a, 2003a, 2005). The DSM-IV-TR (2000) has continued the tradition started in the DSM-III-R (1987) of including dyspareunia as a sexual pain disorder, defining it as a "recurrent and persistent genital pain associated with sexual intercourse" (p. 556). This definition stresses the behaviour that causes pain (intercourse) and that brings many women to clinical attention. Definition of dyspareunia and even its real entity as a "sexual dysfunction" have been challenged (Binik et Al, 2002; Binik 2005, Pukall et Al. 2005). The object of the contention is the "real" nature of dyspareunia, as a complex sexual disorder, encompassing a sexual behaviour precipitating pain (Graziottin, 2005), *or* as a "pure" pain disorder (Binik, 2005). Dyspareunia is a provoked symptom when penetrative sex

causes pain. Without sex, pain is absent, although it may be evoked by other types of vaginal penetration (with finger or objects), including the gynecological examination, or the tampon use (Graziottin et Al, 2001a, Bergeron et Al, 2001, Bouchard et Al, 2002, Harlow et Al 2003) that physically and symbolically mimicks what is feared or is damaging. Vaginal penetration is the *precipitating* factor eliciting pain when a very heterogeneous set of *predisposing* conditions is in play (Graziottin & Brotto, 2004, Graziottin et Al, 2004b).
The aim of this paper is to present to clinicians an overview of etiology and pathophysiology of sexual pain disorders in adolescents. Dyspareunia will be considered according to the established definition (ie, considered a sexual pain disorder) and the reader is referred to the recent literature on the topic for a detailed discussion on current controversies.

VAGINISMUS

Vaginismus is a controversial sexual disorder (Duddle, 1977, Lamont, 1978, Reissing et Al, 1999, Leiblum 2000, Kaneko 2001, Reissing et Al, 2003, 2004, Graziottin et Al, 2004b). It made its first appearance in the DSM-III-R (1987) and has been present in all versions of the DSM since then, including the most recent (2000). Vaginismus is defined as a "recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with intercourse" (p. 558). The definition of vaginismus is currently challenged as well. The key point of the discussion is the real existence of the "involuntary spasm" of the levator ani (Van der Velde et Al, 2001, Reissing et Al, 2003, 2004, Pukall et Al, 2005). From the behavioural point of view, vaginismus classically was characterized by two criteria: 1) the muscular component of the disorder, namely the defensive contraction of the pelvic floor, and 2) the associated fobic behaviours of different intensity. These criteria were well summarized by John Lamont (1978) in his descriptive classification (Tab.1), that still deserves to be mentioned because it is easy to use in the clinical setting, even by the gynecologist not specifically trained in sexual medicine. In its milder degrees, vaginismus allows penetration, although with introital pain: it causes therefore dyspareunia. If intercourse is accepted in spite of pain, the microabrasions intercourse may cause when penetration is performed whithout adequate lubrication (ie vaginal dryness because of poor arousal (Levin 2002) and/or pain) and/or because of elavator ani hyperactivity that further narrows vaginal introitus, may contribute to dyspareunia and/or maintain vulvar vestibulitis (Abramov et Al, 1994, Graziottin et Al 2004b).In its most severe form (degree IV and XO, according to Lamont) intercourse becomes impossible. From the clinical point of view, a continuum therefore seems to exist between lifelong vaginismus and dyspareunia (Kaneko, 2001)

PREVALENCE OF SEXUAL PAIN DISORDERS IN ADOLESCENTS

Dyspareunia, the most common sexual pain disorder, affects 12-15% of women in their life-time. (Laumann et al, 1999). Vulvar vestibulitis (VV), a chronic regional pain syndrome, is the leading cause of dyspareunia in the fertile age (Graziottin, 2001a, Graziottin & Brotto 2004). When vulvar pain, spontaneous and/or provoked by any kind of vulvar touch (intercourse, gynecological examination, attemp to tampon insertion, foreplay) has no obvious objective finding, the term of vulvodynia is preferred.. A recent population-based study has documented that 16% of 4.915

Table 1 - **Severity of vaginismus**

grades	
I	Spasm of the elevator ani, that disappears with patient's reassurance
II	Spasm of the elevator ani, that persists during the gynecologic examination
III	Spasm of the elevator ani and buttock's tension at any tentative of gynecologic examination
IV	Mild neurovegetative arousal, spasm of the elevator, dorsal arching, thighs adduction, defense and retraction
XO	Extreme defense and neurovegetative arousal, with refusal of the gynecologic examination

modified from Lamont JA, Am J Obstet Gyn 131: 632, 1978

women aged 18-64 experienced a chronic, knife-like vulvar pain upon contact (Harlow & Stewart 2003). Precise data on adolescents younger than 18 are lacking. However, cases of vulvar pain in enuretic adolescents, prior to any form of genital intimacy, and/or worsening during foreplay in virgin girl are increasingly reported.

ETIOLOGY OF SEXUAL PAIN DISORDERS IN ADOLESCENTS

According to current classifications criteria (Basson et Al, 2000, 2003), every sexual disorder should be qualified according to key descriptors: the temporal nature (lifelong versus acquired); the context-dependent characteristics (generalized versus situational); the etiology (biological, psychosexual, relational or mixed) and the degree of distress (mild, moderate, severe) the disorder causes to the woman.

Vaginal receptiveness is a prerequisite for intercourse. This ability requires *anatomo-functional integrity* of the many tissue components, both in resting and aroused state (Graziottin, 2003a). Normal trophism, mucosal and cutaneous, normal vaginal and vulvar ecosystems, adequate hormone tissue level, lack of inflammation, particularly at the introitus, normal tonicity and activity of the perivaginal muscles, levator ani first, vascular, connective and neurological integrity, and normal immunitary response are credited to be the necessary conditions to guarantee the vaginal "habitability" (Graziottin, 2001a, 2003a). Vaginal receptiveness may be further modulated by psychosexual, mental and interpersonal, factors: the woman's *motivation* to intercourse is key. Etiology of dyspareunia may be biological, psychosexual and context-dependent (Table 2). (Friedrich, 1987; De Lancey et Al, 1993; Glazener, 1997; Wesselmann et Al, 1997; Graziottin, 2001, 2003a, 2003b). Usually multiple causes are present in the individual patient.

The early diagnosis is key in adolescents, as different conditions contributing to or causing perineal, sexual and/or urogenital pain may overlap. When not diagnosed, they may become major contributor of chronic pelvic pain.

Factors contributing to sexual pain disorders may be classified as **predisposing, precipitating** and **maintaining**. They can also be biological, psychosexual, relational or mixed (Tab.2).

Table 2 - **Etiology of dyspareunia. Many causes may overlap or be associated with coital pain with complex pathophysiologic interplay. The relative weight of each cause in the individual woman may change with chronicity of pain and progressive involvement of other pelvic organs**

A) Biological

a) superficial/introital and/or mid-vaginal dyspareunia

- infectious: vulvitis, vulvar vestibulitis, vaginitis, cystitis
- inflammatory, with mastcell's up-regulation
- hormonal: oral contraception, premenstrual flares
- anatomical: fibrous hymen, vaginal agenesis
- muscular: primary or secondary hyperactivity of levator ani muscle
- iatrogenic: poor outcome of genital surgery; pelvic radiotherapy
- neurologic, inclusive of neuropathic pain
- connective and immunitary: Sjogren's syndrome
- traumatic: Female Genital Mutilation
- vascular: diabetes

b) deep dyspareunia

- endometriosis
- pelvic inflammatory disease (PID)
- pelvic varicocele
- chronic pelvic pain and referred pain
- outcome of pelvic or endovaginal radiotherapy
- abdominal nerve entrapment syndrome

B) Psychosexual

- co-morbidity with desire and /or arousal disorders, or vaginismus
- past sexual harassment and/or abuse
- affective disorders : depression and anxiety
- catastrophism as leading psychologic coping modality

C) Context or couple related

- lack of emotional intimacy
- inadeguate foreplay
- couple' conflicts; verbally, physically or sexually abusive partner
- sexual dissatisfaction and consequent inadequate arousal
- poor anatomic compatibility (penis's size and/or infantile female genitalia)

A) Etiology of dyspareunia

1)According to this perspective, in *adolescents* major etiological factors *predisposing to dyspareunia* may be summarized in:

a) Lifelong conditions, further divided in:

- *biological*: pre-existing vulvar vestibulitis (rare); hyperactive pelvic floor, a condition increasingly recognized as common denominator of relevant comorbidity between urogenital and sexual pain disorders, even in adolescents (McKay 1992; McKay et Al, 2001; Graziottin et Al 2004a, 2004b); rigid/fibrous or cribrous hymen; outcome of Female Genital Mutilation (FGM); Rokitansky syndrome; primary amenorrhea; iatrogenic (outcome of genital surgery, pelvic radiotherapy in childhood etc) (Graziottin 2001b, Graziottin & Basson, 2004) .

- *psychosexual*: vaginismus (of mild/moderate severity, which allows penetration but causes pain) (Lamont 1978, Abramov, 1994, Kaneko, 2001); low sexual desire; inadequate/absent central and/or genital arousal, causing inadequate lubrication or frank vaginal dryness; previous sexual abuse (Ward & Ogden, 1994; Leiblum, 2000, Reissing et Al, 2003);
- *relational*:inadequate foreplay, poor attention to the emotional aspect of sexual intimacy (Basson 1996, Leiblum, 2000), poor erotic skill of the partner; genital dimensional poor compatibility

2)*Acquired* conditions, further divided in:

- *biological*: vulvar vestibulitis & vulvodynia (Paavonen, 1995) , one of the most frequent etiologies of dyspareunia in the fertile age, particularly in young women (Harlow & Stewart, 2003); recurrent vaginitis; vaginal dryness in hypoestrogenic conditions: functional amenorrhea (Graziottin, 2003); puerperium, in adolescent pregnancies (Glazener, 1997); iatrogenic: episiorrhaphy (Glazener 1997), radical surgery, pelvic radiotherapy, vulvar laser therapy (for HPV) (Graziottin 2001b); neurological: multiple sclerosis, nerve entrapment syndrome (Shafik, 1997); vascular: diabetes; acquired defensive hyperactive pelvic floor (Travell & Simons). This latter deserves a special comment as pain and the reported difficulty in using internal vaginal protection (tampon) from the first attempt is significantly higher in women affected by vulvodynia (Harlow et Al, 2004. This symptom could be the earliest sign of hyperactivity of the pelvic floor in adolescents, before their first intercourse. It should alert the physician to recognize this condition and potential associated co-morbidities (Laumann et Al, 1999): dyspareunia, vulvar vestibulitis, bladder symptoms (recurrent cystitis, urge incontinence) and/or constipation, leading to appropriate diagnosis and treatment (Graziottin et Al, 2004a).
- *psychosexual:* low sexual desire/interest; inadequate/absent central and/or genital arousal; body image issues, associated or not with binge eating disorders; sexual abuse (Ward & Ogden, 1994; Edwards et Al, 1997, Leiblum, 2000, Sackett et Al, 2001, Reissing et Al, 2003);
- *relational:* couple conflicts inhibiting sexual desire, motivation and arousal, loss of love/romance reducing responsiveness to sexual cues, inadequate foreplay, penis' dimension (van Lankveld et Al, 1996, Leiblum, 2000).

B) Etiology of vaginismus

Vaginismus may be psychogenically triggered by fear of penetration of whatever conscious or unconscious etiology (Basson, 1996, Ward & Ogden, 1994). The increased muscular tension in the pelvic floor may be part of a systemic arousal response (van der Velde et Al, 2000). A second hypothesis consider vaginismus as a sign of primary muscular neurodystonia, at least in the most severe cases (IV degree according to Lamont) when spontaneous hyperactivity of the levator ani with paradoxical muscle activations has been demonstrated with needle electromyography (Graziottin et Al, 2004a). In the last published classification (Basson et Al, 2003), vaginismus is defined as "The persistent or recurrent difficulties of the woman to allow vaginal entry of a penis, a finger, and/or any object, despite the woman's expressed wish to do so. There is often (phobic) avoidance and anticipation/fear of pain". The muscular component, previously included (Basson et Al, 2000), has been deleted in the last classification (Basson et Al, 2003). It should be reconsidered given the last electromyographic evidence (Graziottin et Al, 2004a). Vaginismus is

one of the leading causes of *lifelong* sexual pain disorders in adolescents. When severe, vaginismus is the leading female cause of unconsummated marriages (Plaut et Al, 2004).

VULVAR VESTIBULITIS

Vulvar vestibulitis is the currently most frequently diagnosed cause of dyspareunia in adolescent. The disorder is acquired in the majority of patients. It is a challenging clinical picture that every gynecologist should diagnose, the sooner the better.

As a syndrome, VV is a heterogenous, multifactorial and multisystemic disease (Graziottin & Brotto, 2004). The diagnostic triad includes: 1) severe pain upon vestibular touch or attempted vaginal entry; 2) exquisite tenderness to cotton-swab palpation of the introital area (mostly at 5 and 7, when looking at the introitus as a clock face); 3) clinical findings limited to vestibular erythema in some women without evidence of an active dermatoses (Friedrich 1987). The areas most often affected include the mucosa around the opening of Bartholin's gland ducts and the posterior aspect of the vestibule. The hymenal sulcus and the paraurethral glands are frequently involved and characterized by tenderness and thickening of their posterior part.

As a multisystemic disease, VV involves:

a) the *mucous structure of the vestibule*, where an intense inflammatory reaction mediated by the *mast cells* has been recently documented (Bornstein et Al. 2001, 2002, 2004). Immunohistochemical staining for tryptase is the most accurate technique for identifying tissue mast-cells (Theoharides et Al, 2001; Bornstein et Al, 2004), proven to be significantly increased in the superficial layers of the vestibular mucosa ($p<0.0001$), more than in the deep layers ($p<0.001$) in comparison to controls. A parallel significant increased activity in production, storage and release of multiple mediators has been proven. The number of degranulated mastcells, is significantly higher ($p<0.0001$) than in controls as well. (Bornstein et Al2001, 2004). Chronic inflammation may be responsible for the increased thinning and frailty of the introital mucosa.

b) the *immunitary system*: *mast-cells' up-regulations* leads to production of chinines, substance P, and other inflammation mediators that cause vasodilatation, oedema, swelling, reddening of the mucosa, burning and pain. The mastcell's productions of Nerve Growth Factor (NGF) (Aloe et Al 1993), stimulates nerve sprouting, and neural hyperplasia, with the *proliferation of pain nerve terminals*, leading to increased pain perception ("hyperalgesia"). The fiber's deeper penetration into the most superficial layers of the vestibular mucosa, which determines the shift from tactile to burning sensations ("allodynia"), has been histologically described (Bohm-Starke 1999, Bornstein et Al. 2004). Mast-cells may play a critical role as a bridging system between a local chronic inflammation (Graziottin et Al, 2004b), of whatever etiology, and the local chronic up-regulation of the pain system, mediated by NGF (Bohm-Starke et Al.1999, Westrom et Al. 1998, Theoharides et Al., 2001). Mast-cells are triggered to degranulate in a differentiated way (ie not all the vescicles release their content at the same time) by different agonist stimuli (Theoharides et Al, 2001). This further contributes to the heterogeneity of the clinical presentation and associated factors (Graziottin et Al. 2004b). Infections (Candida albicans first) (Graziottin et Al, 2001a,2001b, Graziottin, 2003a); mechanical traumas (inclusive of coital rubbing when the lubrication is inadeguate or absent) (Graziottin e Brotto, 2004); estrogens (responsible for the premenstrual flares (Fisher & Bradford, 2002); chemical

and physical stimuli, allergenic substances may all trigger the mastcell's release of substances promoting the subjective and objective features of inflammation (reddening, swelling, increased local temperature, pain and impaired function, in this case sexual intercourse).

c) the *nervous system,* namely *pain fibers and ce*nters. A critical aspect of VV when it becomes chronic is the shifting from *nociceptive to neuropathic pain*. Pain is first a symptom of an ongoing inflammation and damage ("nociceptive"), from which the organism is trying to withheld and to cope with (Bonica, 1990). Over time, when it becomes chronic, pain is increasingly generated by pain fibers and centers themselves ("neuropathic") (Woolf 1993, Baron et al, 2002). It may concur to the persisting inflammation ("neurogenic inflammation"), through a neurogenically induced degranulation of mast-cells, when the stimuli move backwards along the sensory nerves (Bohm-Starke et Al, 1999, 2001a, 2001b). Hyperalgesia may depend as well on the sensitization of thermoreceptors and nociceptors in the vestibular mucosa (Bohm–Starke et Al. 2001b) This may contribute both to the *lowering of the peripheral pain threshold* and to the *increasing production of pain signals travelling from the periphery to the brain* (Lowenstein et Al, 2004). In parallel, a *lower systemic pain threshold* has been described (Pukall et Al. 2002). The up-regulation of the pain system up-regulate the adrenergic system, thus activating the neurovegetative changes (Granot et Al, 2001) that may concur to the hyper-perception of pain, to a "defensive" contracted postural change and to changes in the systemic pain threshold. The connections between the pain polysynaptic pathway with the adrenergic and serotoninergic pathways within the Central Nervous System may explain the neurobiology of co-morbidity with depression and anxiety that chronic VV pain may cause (Asmudson, 2002, Aikens et Al, 2003).

d) the *muscular system:* pain usually activates a defensive contraction of muscles in the painful area, to minimize the risk of further damage (Travell & simons, 1983; Weiss, 2001, Alvarez & Rockwell, 2002). Defensive contraction of the levator ani can be lifelong, when associated to vaginismus, or acquired, in response to persistent introital pain and dyspareunia (Graziottin et Al.2001). Psychosexual factor may further trigger muscle's contraction, leading to myalgia and contributing to the muscular component of pain and VV. In our series of VV patients*, lifelong dyspareunia* was reported by 29% of patients, suggesting that psychosexual factor may precede VV in at least one-third of patients (Graziottin et Al 2001). In 9.7% lifelong dyspareunia was associated with a phobic attitude towards intercourse, which suggests vaginismus as a predisposing factor to muscle hypertonus and VV in this subset of patients, as Abramov first suggested in 1994. Spontaneaous hyperactivity of the pelvic floor was recently documented with needle electromyography in 77.7% of severely vaginismic women, with a further increase of it at straining, opposite to normal. This suggests a primary neurodystonic muscular pathology in this subset of patients (Graziottin et Al. 2004a). Quite interestingly, the same muscular pattern was found in patients with VV who reported a lifelong dyspareunia with phobic attitude towards intercourse. This subset of women, likely to be suffering from vaginismus, reported to have accepted a very painful intercourse for loving reasons and/or not to disappoint their partner (Graziottin et Al, unpublished data). In these cases, the mechanical trauma of intercourse with a dry vagina and a restricted tightened introitus may have precipitated the chronic mucosal damage leading to inflammation and VV. In the pelvic floor, a persistent defensive contraction of the *levator ani,* in response to VV associated pain and dyspareunia, may lead to frank *myalgia* (Weiss, 2001 Alvarez & Rockwell, 2002). Two clinical signs confirm this further contributors to VV pain:

a) "*tender points*", points of acute, localized tenderness at digital contact, at the insertion of the levator ani at the ischiatic spine, found in 56% of our patients (Graziottin et Al 2001d);

b) *trigger points*, point of tenderness which trigger an *acute, irradiating pain*, deep in the pelvis, both to be researched during accurate gynecological examination, aiming at describing the "*pain map*" (Graziottin et Al 2001d; Alvarez e Rockwell, 2002; Graziottin & Brotto, 2004), when the examining finger explores the insertion of the levator ani at the ischiatic spine and other regional muscles, again a diagnostic manouver in common with Interstitial Cystitis (IC) patients (Weiss, 2001).

e) the *hormonal systems*. VV is typical of the fertile age. Cyclical pre-menstrual flares have been reported in a subset of VV patient (another feature in common with IC patients). Estrogen hypersensitivity has been hypothesized (Fisher e Bradford, 2001, Eva et Al, 2003). Estrogens have been demostrated to be agonist ie triggering factors of mastcell's degranulation.

f) the *vascular system* is as well activated in chronic inflammation.. The vestibular erythema is the epiphenomen of superficial vasodilatation mediated by the calcitonin gene-related peptide (CGRP) (Bohm Starke et Al, 1999) released from normally mechanoinsensitive C-nociceptors, which can cause vasodilatation and axon reflex flare even at very low level of activity. "Neurogenic inflammation" describes the acute vasodilatation mediated by nerves signals that move backwards along the sensory nerves and may trigger both mastcell's degranulation and vasodilatation.

The diagnosis should recognize the severity of each system's involvement in the individual woman, to address treatment with a multimodal approach (McKay 1992, Glazer et Al, 1995, McKay et Al 2001, Graziottin & Vincenti, 2002, Vincenti & Graziottin, 2004, Graziottin & Brotto, 2004)

PREDICTORS OF VULNERABILITY TO VULVODYNIA IN ADOLESCENTS

a) pain at tampon use

Vulvar vestibulitis and vulvodynia, leading to dyspareunia, are associated with increase difficulty in tampon use, data varying between 43.5% (Graziottin et Al, 2001d) and 65.8% (Bergeron et Al, 2001). A strong association was reported between pain and difficulty with first tampon use in adolescents and risk of vulvodynia later in life (Harlow et Al 2003). In his study on 137 cases of vulvodynia and 137 controls, Harlow (2004) reported that no pain and little or no difficulty was reported in 39.10% of cases and 60.9% of controls. Pain and difficulty with first tampon use was reported in 60.90% of cases of vulvodynia and 33.9% of controls ($p<0.0001$).The difficulty in tampon use could be consequent to an hyperactive pelvic floor, as a predisposing factor to both subsequent vulvodynia and dyspareunia (Graziottin et Al, 2004a). Indeed an almost constant finding in dyspareunia is the associated contraction of the pelvic floor muscles (De Lancey, 1993; Graziottin 2001, 2003) which is defined as "hyperactivity", through needle electromyography of the levator ani (Graziottin et Al, 2004a). Non-genital, non-sexual causes, such as anorectal problems (anismus, hemorroids, rhagads) or urological factors (in association with urinary tract symptoms, cystitis first, urge incontinence second) are often associated to the levator ani hyperactivity (Wesselmann et Al, 1997). Latent classes analysis of sexual dysfunctions by risk factors in women indicate that *urinary tract symptoms* have a RR = 4.02 (2.75-5.89) of being

associated with arousal disorders and a RR=7.61 (4.06-14.26) of being associated with sexual pain disorders, according to the epidemiological survey of Laumann et Al., 1999. This unsuspected and often overlooked association may be of special relevance in adolescents. Whatever the agonist stimulus – infectious, inflammatory, neurogenic, mechanic, hormonal or chemical – that triggers the mastcell's release and up-regulation (Aloe et Al, 1993, Theoarides et Al, 2001) the common outcome is the maintenance and worsening of local inflammation and tissue damage. This is paralleled by the up-regulation of the pain system, mediated by the mast-cell's production of Nerve Growth Factor (NGF) (Aloe et Al, 1993). The pathoplasticity of the pain systems may contribute to the shift from nociceptive pain (indicator of threatened or ongoing tissue damage) to neuropathic pain (generated in up-regulated fibers and centers of the pain system).

b) oral contraceptives and vulvodynia

Does pain with first tampon use impact on subsequent use of oral contraceptives (OC)? The best study on this controversial association was again carried out by Harlow (2004). Among patients complaining of vulvodynia, no oral contraceptive use was reported in 33.9% of those who did not report pain or difficulty at first tampon use, and 62.7% of who those who did report such difficulty. Any OC's use before the vulvodynia diagnosis was reported in 66.1 of those who did not complain of pain with tampon use and 37.3% of those who did ($p< 0.0008$). In controls, no significant difference was found between previous OC users and no users. Given the strong association between OC'use and vulvodynia, Harlow further investigated to what extent pain with first tampon use influences a woman' decision to use OC. He tried to assess the indipendent effect of OC use on risk of vulvodynia focusing on women who never experienced pain with first tampon use. When researcher assessed ever vs never use of oral contraceptives, without taking into account whether or not use of OC's came before or after first onset of vulvar symptom, they found a strong association (OR 2.6, CI 1.1-6.3). However, when the Author considered use of OC only before the first onset of vulvar pain symptoms, in vulvodynia patients, and a similarly matched time period for controls, they saw little overall association. Further dividing women in two age classes, oral contraceptive's use was reported in 40.2% of cases and 41.6% of controls (OR=1.0, CI 0.4-20) among those older than 18. In those younger than 18, OC's use was reported in 10.2% of cases and 3.7% of controls (OR 4.1, CI 1,0-17.7). Women who had little difficulty with tampon use early in life, who then went to use oral contraceptives, appears to substantially increase their risk of vulvodynia. The risk was higher among those who began using OC prior to age of 18. According to this research, therefore, the association between OC and vulvodynia is applicable only to that subgroup of women who develop vulvodynia with no early genital pain.
This research helps to clarify the heterogeneity of predisposing and precipitating factors in vulvar vestibulitis and vulvodynia, contributing to a better understanding of its natural history (Graziottin & Brotto, 2004). In women who have pain at first tampon use, the hyperactivity of the pelvic floor (either primary or associated with fear of penetration, mild vaginismus, and/or poor mental and genital arousal) seems to be the leading predisposing factor to dyspareunia and intercourse-associated introital mucosal damage contributing to vulvar vestibulitis. For women with no such difficulty with tampon use, who developed acquired dyspareunia and vulvodynia *after* OC use, particularly when younger of 18, the predisposing role could be the inadequate genital arousal reported in on average one fifth of OC users, particularly with ultralight pills (Caruso et Al, 2004). The consequent vaginal dryness could predispose to coital mucosal microabrasions, triggering

both mast-cell's up-regulated degranulation and a secondary hyperactivity of the pelvic floor. This could then contribute to both dyspareunia and vulvar vestibulitis (Graziottin et Al, 2004a). It may explain the co-morbidity between dyspareunia and vulvar vestibulitis: dyspareunia is respectively reported as lifelong in 29.0% and as acquired in 61.3% of the Author's patients (Graziottin et Al, 2001).

Medical ("organic") factors - too often underevaluated in the clinical setting - are therefore the most frequent and important causes of dyspareunia in adolescents. They may interact with psychosexual factors. A thorough medical evaluation is therefore mandatory.

CLINICAL PRESENTATION

Vulvar vestibulitis is more frequently complained of in young patients, in their fertile years. In our series, evaluated in 2001, mean age was 31.73 (range 17-48 yrs). 88,7% were nulliparous. Mean duration of symptoms was 57,43 months (range 1-336 months), this lag time between onset of symptoms and VV diagnosis being another feature in common with IC. In spite of the long lasting duration of symptoms, and multiple gynecologic and/or urologic visits, 75,80% had the first diagnosis of VV only at the moment of the present consultation (Graziottin et Al, 2001b). 22,50% were diagnosed of VV and treated elsewhere with persisting symptoms (19,35% having both VV and recurrent cystitis). Dyspareunia was reported as lifelong in 29,0%; acquired in 61,3%, intermittent in 9.7% Etiology appear to be mixed in all cases, as organic/biologic factors interact with psychosexual ones: 58,1% had a documented history of chronic candidiasis (vs 5-8% prevalence in the general population (Sobel et Al, 2004), usually secondary to repeated antibiotic treatments; 33,9% had positive swabs for bacterial infections, most gardnerella or mixed; 11,3% had a history of vulvar Papillomavirus. Sexual harassment in childhood or adolescence was reported in 24,19% with penetrative abuse in 6,45%. (Graziottin et Al, 2001c).

In a recent review of our cases (Graziottin 2005, unpublished data), an increase in younger adolescents was noted, due to an increase of referrals from other colleagues. 19 patients out of 412 (4.85%) were younger than 18; 6 out of 19 (31%) had no sexual experience. Of them, 2 had a history of nocturnal enuresis, urine acting as a local irritant, 4 had positive swabs for recurrent candida. The leading motivation for referral was dyspareunia (6/19), vulvodynia and dyspareunia (5/19), vulvodynia (8/19). 7 never tried tampon use. Of the 12 who did, all but two experienced difficulty at tampon insertion (83.34%). Only 3/13 (23%) of those sexually active were using oral contraceptives.Their use was antecedent to the onset of symptoms. 4 adolescent reported childhood invasive diagnostic manoeuvers (three urethral swabs, one vaginal swab) that were experienced as extremely painful and frightening. All patients had the symptoms and signs of vulvar vestibulitis (Friedrich 1987), which was co-morbid with vaginismus in 7 (three of IVth degree, 4 of IIIrd degree, according to Lamont). Vulvar vestibulitis should be considered in the differential diagnosis of adolescents complaining of dyspareunia, impossibility to intercourse, vulvodynia and/or pain or difficulty in tampon use. Principles of treatment when dyspareunia is complained of are summarized in Table 3.

TALKING WITH ADOLESCENTS ABOUT SEXUAL ISSUES

Sexual pain disorders are difficult to disclose, specially by adolescents, who often need their parents approval before asking for a gynecological evaluation. Vulvodynia is somehow easier to report., as it does not immediately convey a sexual meaning. A proactive, empathic approach to the adolescents sexual life will convey an attitude of availability and acceptance. Sexual issues may be discussed in a number of contexts, including: a) obtaining background information about sexual function; b) addressing possible consequences of illness, injury, procedure or medication; c) presentation by the patient of a sexual problem or question.

The sexual history is the core of the clinical report when sexual pain disorders and/or vulvodynia are complained of. It requires a sensitive approach (Tab. 4): at any age it takes courage to disclose a sexual dysfunction or a sexual trauma. More so in adolescents. Such disclosures should be taken seriously and appropriately addressed. Adolescents have diverse experiences, values and preferences. The physician should be be sensitive to gender and cultural differences. However, he/she should not assume that any one patient necessarily fits a gender or cultural stereotype.

Whenever possible, both the symptomatic patient and the partner should be involved in evaluation and treatment (Plaut et Al, 2004). Ethical and legal considerations are as well worth of special attention in adolescents complaining of sexual problems. Confidentiality, but also any legally or ethically imposed limits on confidentiality itself, should be discussed. Adolescents should be informed about the limits privacy has when risky physical and/or emotional situation are disclosed/complained of in the clinical setting. Legal and procedural requirements regarding patient consent should be observed. Last but not least, appropriate boundaries with the patient should be respected, together with the patient's needs for privacy and modesty (Plaut et Al, 2004)

Table 3 - **Treatment of dyspareunia in adolescents**

• Address predisposing, precipitating and maintaining etiologic factors, either biological and/or psychosexual, taking a collaborative approach where possible
• Treat recurrent vaginitis and/or cystitis or other associated urinary tract or proctologic symptoms
• Restore normal vaginal trophism with topical estrogens if indicated (eg in case of dysfunctional amenorrhea) (always record the vaginal pH!)
• When hyperactivity of the pelvic floor is diagnosed, teach relaxation techniques, focused on the pelvic floor muscles, inclusive of local vaginal self-massage.
• When myalgia of the pelvic floor is diagnosed with tender and/or trigger points on the levator ani, either physiotherapy and/ or electromyographic vaginal biofeeback, may significantly reduce both the contraction and the associated muscular pain.
• If VVS is diagnosed, treat the pertinent predisposing, precipitating and maintaining factors
• Depending on the nature of pain (nociceptive or neuropathic), address the pain disorder with topical electroanalgesia or specific systemic (amytriptiline, gabapentin) and/or local antalgic treatments; vestibulectomy is to be reserved to chronic VVS that is not responsive to the above treatments

modified from Graziottin 2004, with permission

Table 4 - **Talking with adolescents about sexual issues**

• Be sensitive to the optimal time to ask the most emotionally charged questions
• Look for and respond to non-verbal cues that may signal discomfort or concern
• Be sensitive to the impact of emotionally charged words (e.g. 'rape', 'abortion')
• If you are not sure of the patient's sexual orientation, use gender-neutral language in referring to his or her partner
• Simply explain and justify your questions and procedures
• Teach and reassure as you examine: use a mirror to explain genital anatomy and to show how to recognize the contracted/relaxed state of the pelvic floor, visually and from the proprioceptive point of view
• Explain how to voluntarily relax the pelvic floor, and to push correctly, before the gynecological examination and any invasive manouver (like inserting the speculum)
• Intervene to the extent that you are qualified and comfortable; refer to qualified medical or mental health specialists as necessary

Modified from Plaut et Al, 2004

CONCLUSION

Sexual pain disorders are caused by a heterogeneous, multisystemic and multifactorial set of conditions. The biological etiology of these complaints should be diagnosed without treating the adolescent's genital pain as "psychogenic". Pain at first tampon use could be a warning symptom of the hyperactivity of the pelvic floor, that can be both a predisposing and maintaining factor of dyspareunia in adolescents. Vaginal dryness and/or genital arousal disorders, specially after onset of OC 'use, should be considered and appropriately addressed. Invasive manoeuvers, at any age, should be performed in a sensitive way, always explaining how to relax the pelvic floor before initiating any of them, even the most apparently innocuous ones like a urethral or a vaginal swab.

Predisposing, precipitating and maintaining factors, biological and psychosexual, should be diagnosed. They contribute to the individual vulnerability to sexual pain, which is elicited when the precipitating event - vaginal penetrative sex - is attempted or accomplished.

Addressing the complexity of the etiology is critical for a multimodal treatment of sexual pain disorders in adolescents. Therapeutic strategies should progressively move from a symptomatic, pragmatic approach to one more pathophysiologically oriented.

Finally, a sensitive and supportive doctor–patient relationship is key. The adolescent (and the couple, if she has a stable relationship) needs desperately to feel that her pain is trusted, respected and investigated as a serious medical problem. This is the basis for an effective therapeutic alliance and a powerful healing factor, to help adolescents with sexual pain disorders "to feel normal" again.

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