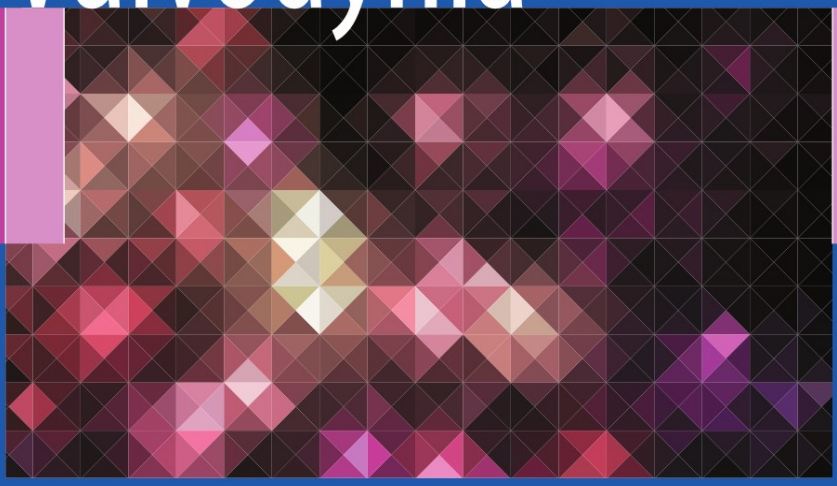
Alessandra Graziottin
Filippo Murina

Clinical Management of Vulvodynia



Tips and Tricks

Springer

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Alessandra Graziottin · Filippo Murina

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Preface

Why a Book About Vulvodynia? And why "Tips and Tricks"?

Why this book? Women have an intimate problem: chronic vulvar pain, or vulvodynia, as it is termed in medical phraseology. Vulvodynia may affect 12-15% of women: it is therefore a common disorder that every family doctor and every gynecologist can encounter every day in his or her routine work.

The first good reason to write – and read – this book is that although vulvodynia is frequent, it typically remains unaddressed for years. Indeed, this genital pain is neglected by the majority of physicians because it is perceived as difficult to deal with or as "psychogenic" and therefore more of an issue for psychologists than for medical doctors. In fact, in contrast to this outdated view, vulvodynia is a disorder with solid biological causes that are absolutely within the domain of a medical diagnosis.

Like all types of pain, vulvodynia can be multifactorial. Diagnosis requires careful listening to the woman's symptoms, accurate reading of vulvodynia's pathophysiology, a competent physical examination focused on detecting all the clinical signs, and renewed attention to the frequent comorbidities (medical and sexual) that may accompany vulvar pain.

The most frequent medical comorbidities are bladder symptoms (post-coital cystitis, bladder pain syndrome), endometriosis, irritable bowel syndrome, fibromyalgia, and headache. Among the sexual comorbidities, coital pain (dyspareunia) is the leading symptom, with its accompanying cohort of secondary loss of desire, vaginal dryness, orgasmic difficulties, and sexual dissatisfaction that can deeply affect a couple's relationship.

The clinical method for addressing pain of any kind is familiar to every physician: it only requires to be specifically focused on the vulvar area, with a specially sensitive and gentle approach. Why? Because vulvodynia involves the most secret part of the body – the vulva and the introitus of

the vagina – and sometimes it may be difficult to disclose problems in this area even to the most intimate of friends.

Curing vulvodynia can be an extremely rewarding experience, as cure offers the affected woman a real chance of regaining her full level of well-being, with a satisfying intimate life and the possibility of making love again with passion and joy.

Why tips and tricks? To ease the route to a correct diagnosis for every physician who is motivated to help women presenting with genital/vulvar pain. Yes, a physician's life is professionally too busy. We all have little time to update our knowledge, there are multiple issues, and we all need concise, distilled information that will assist us in rapidly understanding the essence of a clinical picture.

This is why we accepted the challenge of writing a "tips and tricks" version of a clinical book: to offer a synthesis of current knowledge that is easy to read and consult, is quick to the point, and will increase physicians' confidence in their ability to make a competent diagnosis and to prescribe effective first-line therapy. With this in mind, practical tips are included in every chapter, in a different color, so that the reader will be able to translate epidemiological or pathophysiological considerations into concrete help in the clinical setting from the outset.

In brief, our goal is to empower physicians to rapidly address vulvodynia and its associated comorbidities. The sooner, the better.

Alessandra Graziottin, MD
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About the Authors

Alessandra Graziottin, MD

Alessandra Graziottin is Director of the Centre of Gynecology and Medical Sexology at the H. San Raffaele Resnati in Milan, Italy. She is Chairman of the "Alessandra Graziottin Foundation for the cure and care of pain in women", which she founded in 2008. Dr. Graziottin has published 15 scientific books (as author, co-author or editor), more than 70 chapters of scientific books, 80 refereed and 240 non refereed papers, 6 lay books and several educational booklets for women. She is Coordinator of the Special Interest Area "Pelvic Pain" and Member of the National Observatory on Sexual Habits and Contraceptive Choices of the Italian Society of Gynecology and Obstetrics (SIGO). She is also Member of the European Working Group of FSDeducation.eu, that develops CME-certified educational material on Female Sexual Dysfunction. She is currently a board member of the Italian Society of Preventive and Social Pediatrics (SIPPS) and Vicepresident of the Italian Society of Psychosomatic Gynecology and Obstetrics (SIPGO). In 2004 she was awarded the Honorary Membership by the Society of Obstetricians and Gynecologists of Canada (SOGC). She has given more than 970 lectures at international and national meetings and courses.

In October 1998 she contributed as a board member to the First International Consensus Conference on Female Sexual Dysfunction, in Boston. In 2003 she assumed this role for the Second International Consensus Conference in Paris. In 2005-2006 she chaired the FSD Committee of the International Society for Sexual Medicine (ISSM). In 2009 she was the European member of the Scientific Program Committee of the XIX World Congress of Gynecology and Obstetrics (Cape Town). In 2010, she was co-President of the National Congress of the Italian Society of Gynecology and Obstetrics (SIGO) held in Milan (November 14-17). Since 1984 she has been regular columnist in Italian health magazines, newspapers and journals. As key opinion leader in Obstetrics, Gynecology and Sexual Medicine, she is regularly interviewed in TV, radio and Internet programs. In 2010 she has been the most interviewed woman in the seven major National TV News programs. Her detailed CV is available at www.alessandragraziottin.it, English Section.

Filippo Murina, MD

Filippo Murina is currently First Referent of the Outpatient Department of Vulvar Disease at the V. Buzzi Hospital of Milan, Italy.

He received his medical degree at the University of Milan in 1989, where he achieved the specialization in Gynecology and Obstetrics in 1994.

Since 2006 he has been Founder and Scientific Director of the Italian Vulvodynia Association (AIV).

He is currently a board member of the Italian Society of Vulvology (SIIV), Fellow of the International Society for the Study of Vulvovaginal Disease (ISSVD) and Member of the European College for the Study of Vulval Diseases (ECSVD).

He was advisor as Reviewer of the European Journal of Obstetrics & Gynecology and Reproductive Biology, the American Journal of Obstetrics and Gynecology, the Journal of American Academy of Dermatology and the Journal of Women's Health.

Dr. Murina has published 6 scientific books (as author, co-author or editor), 80 papers and proceeding contributions; his recent study on vulvodynia therapy has been published on the British Journal of Obstetrics and Gynecology.

As a leading expert in vulvar diseases and vulvar pain, he has given more than 60 lectures at meetings and courses.

Since 2008 he has been regular columnist and advisor in Italian health magazines.

Contents

Epidemiology of Vulvar Pain and its Sexual Comorbidities

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Vulvodynia is not a rare condition. Studies suggest that up to 15% of gynecology clinic populations have the disorder at any given time.

In the United States, up to 15% of all women suffer from chronic vulvar pain, which may be assumed to be vulvodynia, at some point in their lives. Hence, up to 14-million women are affected by vulvodynia during their lifetimes, with the condition accounting for 10-million doctor visits annually. Results from research on the epidemiology (the study of the distribution and causes) of vulvodynia have helped to clarify the magnitude of the problem.

Vulvodynia was first described by Thomas in 1880 as hyperaesthesia of the vulva, that is "excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva".

The prevalence of vulvodynia may be underestimated, partially because some physicians dismiss the problem as being psychological in origin and relatively unimportant. Also, affected women may be reluctant to discuss their symptoms, which they may perceive as unusual and possibly 'all in the mind'.

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In a 2003 survey of 5000 women between the ages of 18 and 64 (3358 surveys returned and analyzed; 67.16% response rate), ***15.6%*** *of respondents reported a history of chronic burning, knife-like or sharp pain, or pain on contact, that lasted for 3 months or longer, at some point during their lives (Harlow and Stewart, 2003).*

As vulvodynia receives increased attention by both the medical profession and the media, however, more women are aggressively seeking care. As a result, a higher prevalence for vulvodynia than had previously been recognized is coming to be appreciated.

A 2001 study of women in the Boston area revealed that chronic burning, knife-like pain, or pain on contact, that lasted at least 3 months or longer in the lower genital tract occurred frequently. These symptoms were reported by White, African American, and Hispanic women of all ages, and nearly 40% of these women chose not to seek treatment. Of the women who sought treatment, 60% consulted three or more doctors, and 40% remained undiagnosed after three medical consultations. These researchers estimated that about 16% of women experience symptoms consistent with vulvodynia in their lifetimes.

Symptom onset was most prevalent between the ages of 18 and 25 years, with lowest prevalence after age 35 years. Compared with controls, women with vulvar pain were seven-times more likely to report difficulty and pain with their first tampon use.

TIP: This complaint, too often dismissed as a minor information, is of the highest clinical importance: it should immediately suggest to evaluate: 1) the hymen, to diagnose more rare anomalies (1%) such as a tighten hymen, cribrous or septum; 2) the levator ani, to exclude or diagnose an hyperactivity of this muscle, contributing to: levator ani myalgia and narrowing of the vaginal entrance, thus contributing to vaginismus and dyspareunia; lifelong obstructive constipation; postcoital cystitis, if the adolescent already has sexual intercourse.

Although women of reproductive age were most affected, it was found that almost 4% of women between the ages of 45 and 54 years, and another 4% aged 55 to 64 years, reported burning or knife-like vulvar pain or pain on contact; in 50% of these cases, pain limited sexual intercourse.

In the USA, various degrees of dyspareunia (difficult or painful coitus) are reported by 21% of coitally active women, and by 10.5% of women between 40 and 80 years (Laumann et al., 1999). In Europe, 14% of women aged between 20 and 70 years reported coital pain (Fig. 1.1).

Lifelong mild vaginismus contributing to lifelong dyspareunia may occur in 10-15% of women. Severe vaginismus, preventing intercourse, may be complained of by 0.5–1% of women in reproductive age, although precise estimates are lacking.

Compared with controls, women with vulvodynia have been shown to be significantly more likely to report chronic medical conditions, including bladder pain syndrome/interstitial cystitis, fibromyalgia and irritable bowel syndrome (IBS).

It has been estimated that among women with urologist-diagnosed interstitial cystitis (IC), more than half (51.4%) were diagnosed with vulvodynia. This strong link may be related to a common etiology for these two conditions. The vulva and bladder are both derived from the embryonic urogenital sinus and share common sacral nerve innervation pathways. Moreover, both the vagina and the urethra are surrounded by the levator ani. Hyperactivity of this muscle, reducing the vaginal entrance and causing coital pain ("introital dyspareunia") may reduce/block the vaginal lubrication and congestion of the cavernous vascular bulb, predispose to recurrent mechanical coital trauma of the vestibular mucosa *and* of the urethra/trigonal area, thus contributing to the bladder pain syndrome and vulvar vestibulitis. Data suggest that women with IC report lifelong dyspareunia and fear of intercourse since adolescence significantly more than controls (Peters KM et al., 2007). Conditions that affect the bladder may therefore lead to symptoms in the vulva, and vice versa.

Between 12% and 68% of patients diagnosed with IBS/IC report vulvodynia symptoms.

TIP: Physicians should routinely ask their vulvodynia patients if they:

- had obstructive constipation since childhood (lifelong);
- had difficulty in inserting tampons since adolescence;
- recall having had coital pain and/or fear of intercourse since the first sexual experiences (lifelong dyspareunia and/or vaginismus);
- suffer from bladder pain symptoms (burning, urge, frequency…);
- have recurrent cystitis 24-72 hours after intercourse ("post-coital cystitis").

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These symptoms cluster key vulvodynia's comorbidites, suggest a common pathophysiologic predisposing factor in the hyperactive pelvic floor and may be addressed with a multimodal treatment aimed at relaxing the pelvic floor (see Chapter 8). This would move patient from comorbidity to co-treatment, thus improving different symptoms and quality of life while saving costs.

Box 1. Vulvodynia and its comorbidities

- 50% of women with irritable bowel syndrome also had interstitial cystitis
- 38% of women with interstitial cystitis had irritable bowel syndrome
- 26% of women with interstitial cystitis also had vulvodynia

Conclusions

Vulvodynia is highly prevalent, affecting 12-15% of women in the lifespan. Coital pain, namely vaginismus and dyspareunia, are the sexual symptoms that most frequently may predispose to vulvodynia, when lifelong, i.e. since the very first sexual experiences; or be consequent to it, when, more rarely, vulvar pain precedes intercourse. Vulvodynia is frequently associated to significant comorbidities (recurrent cystitis/bladder pain syndrome; irritable bowel syndrome; obstructive constipation; endometriosis; and

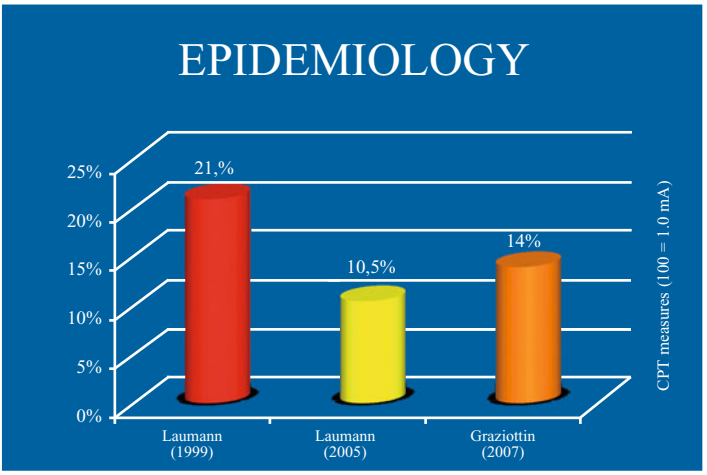

Fig. 1.1 Prevalence of dyspareunia

also headache and fibromyalgia) that should be investigated and addressed in a multimodal multidisciplinary approach. A comprehensive evalution is key for a successful outcome.

Vulvodynia – What's Behind the Name? 2

'Vulvodynia' is a diagnostic term referring to chronic pain in the vulvar area of at least 3 months duration.

Vulvodynia includes and encompasses a number of heterogeneous vulvar conditions, with different etiologies and pathophysiologies, and a common symptom: *chronic vulvar pain*.

Characteristics and Etiology of Vulvar Pain

Vulvodynia may be chronic or unremitting, intermittent or episodic (often exacerbated premenstrually). It may be unprovoked (spontaneous) or it may occur only in response to a touch stimulus (provoked pain), including tight clothing or physical stimulation in the vulvar area (such as with coitus or pelvic examination). It may be generalized, involving all the vulvar area, or localized, limited to the vestibular area (defined as 'vulvar vestibulitis', or VV), to the clitoris ('clitoralgia'), to the peri-urethral mucosa and/or to a limited part of the vulva (Fig. 2.1).

It may be useful to clinically describe vulvar pain using a 'pain map' that describes the site and the intensity of pain derived from the woman's history, and the symptoms reported by the woman during vulvar and pelvic examination.

There is no consensus about the use of terms to define and subtype

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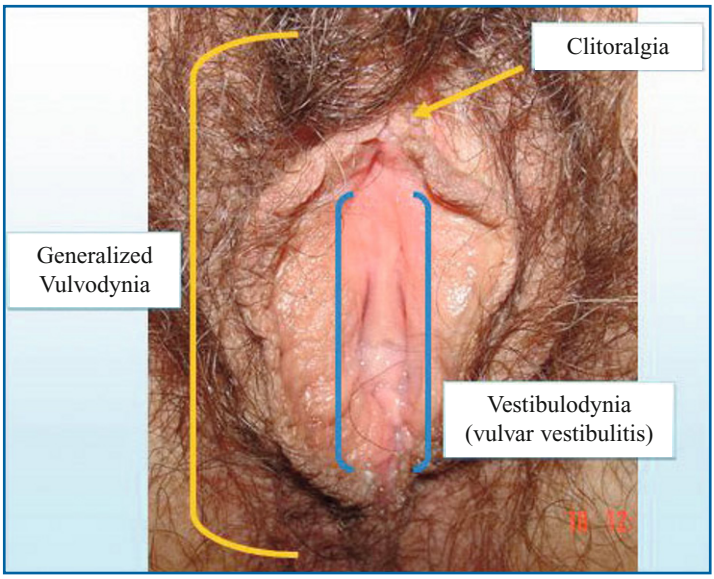

Fig. 2.1 Vulvodynia may be generalized, involving all the vulvar area, or localized, limited to the vestibular area (defined as *vulvar vestibulitis*, or VV), to the clitoris (*clitoralgia*), to the peri-urethral mucosa, and/or to a limited part of the vulva

conditions underlying vulvodynia. However, other descriptors may be clinically useful. For example, vulvodynia can be the only complaint (‘*isolated’ vulvodynia)*, or it may be *comorbid* with other conditions:

1. **Medical**: vulvo-vaginal *Candida* infections, vulvar dystrophies and neoplasms, contact dermatitis, hypoestrogenic and hypoandrogenic atrophy, painful bladder syndrome, endometriosis, irritable bowel syndrome, fibromyalgia, headache. Other recognized medical disorders with a possible chronic vulvar pain component include neurologic etiologies (pudendal nerve entrapment syndrome, multiple sclerosis), referred pain from myalgic muscles (*levator ani*), iatrogenic conditions (painful outcome after perineal surgery such as episiorraphy, hemorroidectomy, or posterior colpectomy), or pelvic/perineal radiotherapy;

Box 1. Iatrogenic Vulvodynia

Iatrogenic factors may act as **predisposing, precipitating and/or maintaining** contributors to vulvodynia:

- **Predisposing factors** include: invasive exams and manoeuvers such as vaginoscopy, cystoscopy, bladder catheterism, suturing of perineal traumatic accidental abrasions without appropriate analgesia, caring and explanations of the type of the exam or maneuver. Pain experienced in these situations, fear and anguish may contribute to a specific vulnerability towards the potential aggressive meaning implicit in vaginal penetration and may contribute to vaginismus, hyperactive pelvic floor and a fobic attitude to intercourse, contributing to lifelong dyspareunia. In the Author's experience, these iatrogenic factors may account as unique genital and emotional traumas for 5.8% of subsequent vulvodynia and dyspareunia.
- **Precipitating factors.** Any medical or surgical intervention on the vulva or vagina when it damages the pudendal nerve endings and/or the anatomy and function of vulvar/introital area. Potential precipitating iatrogenic factors contributing to dyspareunia include:
  - vulvar laser or diatermocoagulation for condilomatosis (genital warts) or for physiological vestibular papillomatosis misdiagnoses as HPV infection. This complication is more frequent when the laser goes too deep in the mucosa, damaging the deeper pain nerve endings and/or when it is repeated;
  - episiotomy/rraphy, when infections, dehiscence of the suture and retracting scars damage the anatomy of the introital area often complicated with a specific damage of the terminal endings of the pudendal nerve;
  - surgery for Bartholin's gland and abscesses, more so when surgery is repeated;
  - anterior and posterior colporraphy, the latter having the highest rate of dyspareunia complications and vulvodynia;
  - anal surgery, for hemorrhoids and ragads;
  - radiotherapy for anal, bladder and cervical cancer;
- **Maintaining factors:** diagnostic omissions of etiologies of vulvodynia/dyspareunia are the most powerful maintaining factors contributing to vulvar pain. Top of the list is the attitude to deny women the real biological etiology of their vulvar pain, that is not "all in their head". A further side effect of this attitude is its negative impact on the partner and family of the woman affected with vulvodynia. This denial of the biological truth of pain may trigger the partner's aggressiveness up to a frank physical, emotional and/or sexual abuse, contributing to depression, anxiety, chronic stress, all factors that worsen the perception of pain and to further fear of being penetrated.

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Key point: Physicians should increase their attention to the potential iatrogenic role implicit in their diagnostic or therapeutic behaviors involving the pelvic organs, vulva and perineum at any age in the lifespan.

2. **Sexual**: coital pain ('dyspareunia') is the most frequently reported sexual problem alongside loss of desire, vaginal dryness, orgasmic difficulties, especially during intercourse. In severe cases, sexual aversion may be reported.

Table 2.1 The characteristics of vulvodynia

Vulvar pain can be:
- Chronic/unremitting or
- Intermittent/episodic

- Spontaneous or
- Provoked

- Generalized or
- Localized - limited to:
  - the vestibular area (*vulvar vestibulitis*)
  - the clitoris (*clitoralgia*)
  - the peri-urethral mucosa
  - a limited part of the vulva

- Isolated or
- Comorbid with:

  Medical conditions:
  - recurrent *Candida* vaginitis
  - painful bladder syndrome
  - irritable bowel syndrome
  - endometriosis
  - fibromyalgia
  - headache
  - anxiety and depression

  Sexual problems:
  - dyspareunia (introital)
  - loss of desire
  - vaginal dryness
  - orgasmic (coital) difficulties
  - sexual aversion

Definitions of Vulvodynia

Definitions of vulvodynia have varied widely, mirroring the difficulties in understanding and substantiating the clinical reality and the pathophysiology

of vulvar pain. Of interest and concern is the fact that the condition was not officially recognized until 1898, was overlooked for more than 80 years, and then resurfaced in gynecological texts in the 1980s. The working definition of vulvodynia used by a 2005 consensus panel was 'chronic pain lasting from three to six months in the vulvar region *without another definable cause.'* The most recent terminology and classification of vulvar pain by the International Society for the Study of Vulvovaginal Disease (ISSVD) divides potential causes of vulvar pain into four categories:

- infectious;
- inflammatory;
- neoplastic;
- neurologic.

Conditions falling into these categories must be ruled out prior to making a diagnosis of vulvodynia, defined as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder." Vulvodynia is not caused by infection (candidiasis, herpes, etc.), inflammation (lichen planus, immunobullous disorder, etc.), neoplasia (Paget's disease, squamous cell carcinoma, etc.), nor is it a neurologic disorder (herpes neuralgia, spinal nerve compression, etc.).

The classification of vulvodynia is based upon the site of the pain, whether it is generalized or localized, and whether it is provoked, unprovoked, or mixed. The ISSVD further classifies vulvodynia as follows:

- Generalized vulvodynia
  - provoked (sexual, nonsexual, or both);
  - unprovoked;
  - mixed (provoked and unprovoked);
- Localized vulvodynia
  - provoked (sexual, nonsexual, or both);
    - *provoked vestibulodynia/Vulvar Vestibulitis Syndrome*;
  - unprovoked;
  - mixed (provoked and unprovoked).

TIP: Unfortunately, these definitions limit vulvodynia to a subset of *unexplained* vulvar pain, thus missing those conditions where pain has a clear etiology. Opposite to that, **we suggest that vulvodynia should include all types of vulvar pain. It is the physician's responsibility to make a differential diagnosis among the different biological**

etiologies of vulvar pain, focusing on pathophysiology and the histology of vulvar tissue. Vulvodynia can be exacerbated by *psychobiological* factors (anxiety, depression, chronic stress, former abuse) and *sexual* triggers such as intercourse.

Indeed, pain (almost) always has a biological etiology (the only exception being pain from grief) and what may not be immediately visible at first vulvar examination may become evident when appropriate and skilled clinical examination is performed and/or when histological data express clear evidence of an inflammatory condition typical, for example, of vulvar vestibulitis.

Impact of Vulvodynia on Physical and Psychosexual Health

Vulvodynia is a prevalent and highly distressing disorder, with major health, psychosexual, interpersonal and social consequences.

- **Health-related issues**: Besides being a serious medical problem, vulvodynia may trigger a process whereby the pain spreads to become a real 'red alert' in the pelvis. As a chronic inflammatory process, vulvar pain may secondarily involve/extend to other pelvic organs: the most frequent comorbidity being with bladder symptoms (post-coital cystitis, bladder pain syndrome). Other significant associations include endometriosis, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, coccygodynia, headache and anxiety/depression. Preliminary evidence suggests a pathophysiology for comorbidities that involves:
  1. **A chronic inflammatory process involving different pelvic organs**. The common denominator seems to be the hyperactivity of mast cells (Fig. 2.2), which produce and release molecules that are responsible for the local inflammatory process, for the activation of the pain system, and for the defensive contraction of muscles in the painful area. Mast cells travel throughout the body, specifically patrolling the body's 'boundaries' such as the colonic mucosa, the bladder mucosa and the vestibular area. They are the powerful directors of the inflammatory orchestra, and the mediators of the shift from acute inflammation with nociceptive pain to chronic inflammation with a further step towards neuropathic pain. This may help to explain how comorbidities arise among organs and systems that are located at different sites;

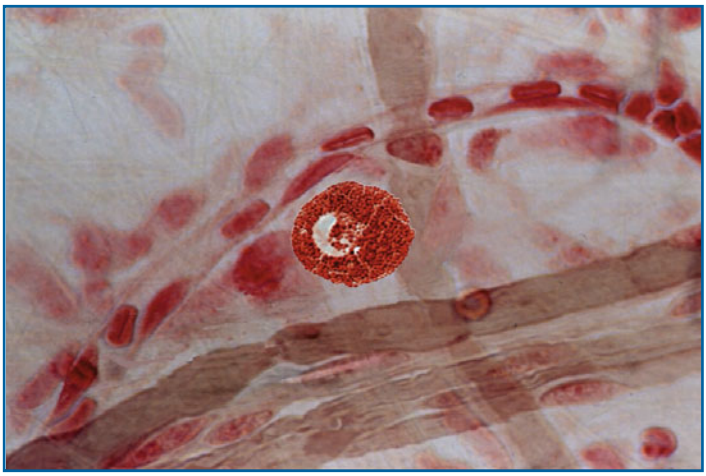

Fig. 2.2 Mast cells picture, rounded elements with an oval nucleus and cytoplasm with spherical granules containing cytokines, growth factors, vasoactive amines and proteolitic enzymes. Mast cells activated by various stimuli selectively release inflammatory factors that mediate the typical signs and symptoms of local inflammation including erythema, edema, increased local temperature, pain and functional impairment. When persistently up-regulated, mast cells maintain chronic inflammation, leading to a shift between nociceptive and neuropathic pain

2. **Nerves innervating the organs that are in close proximity to the vulva** (for example, the pudendal nerve). The term '**cross–talk**' has been used to express this process of 'sharing pain' between different organs sharing a common innervation. Proliferation of the pain nerve endings in the inflammated tissue, mediated and induced by the Nerve Growth Factor (NGF) produced by the hyperactivated mast cell has been histologically proven.
3. **The hyperactivity - i.e. the excessive contraction - of the levator ani**, the key muscle of the pelvic floor. This contraction can be either lifelong ("myogenic") and associated to early symptoms such as lifelong constipation and/or bladder symptoms such as recurret cystitis from colonic germs urge and/or recurrent vaginitis.

- **Psychosexual issues:** having pain in a 'secret' area of the body, difficulties in disclosing it to others, and/or being medically labeled as 'inventing the pain', may trigger a sense of isolation in women - of being 'the only one' with such an embarrassing and disabling condition. This suffering may be worsened if the woman has been harassed or abused in the past: the pain can act as a reminder of what she has suffered; it can be associated with unspecified feelings of guilt or be perceived as 'retribution' for perceived inappropriate sexual desire, masturbation, or affairs; and it can be associated with post-traumatic stress

disorder. As unwanted pain is the strongest reflex inhibitor of desire, of mental and physical arousal, vulvodynia is associated with the progressive inhibition of the sexual response, with low levels of desire, vaginal dryness, orgasmic (coital) difficulties and increasing dissatisfaction or frank frustration with sexual intimacy. Chronic pain, of whatever type, can destroy a person's vitality, leaving the patient weak, fatigued, anergic, moody, fearful, distressed, depressed, and pessimistic to the degree of frank catastrophism, a shadow of the person they once were.

- **Interpersonal and social issues:**
  a) **For the couple**: having a partner who complains of chronic genital pain is a challenge even for the most loving of companions, for a number of reasons: 1) it can chronically limit sexual intimacy up to to the point of frank avoidance of any intimate behavior; 2) it can monopolize the conversation and focus the couple on the vulvar pain and its related symptoms; 3) it can irritate and causes anger, aggressiveness, and frank verbal and physical abuse, especially if the woman's physician tells the partner that: "The pain is all in her head"; that, "She is inventing the pain"; or that, "She is just trying to avoid having intercourse"; 4) it has increasing costs, both monetary (for physician visits, physical examinations, loss of working days) and related to quality of life (the social and emotional impact on a relationship);
  b) **In the family**: when a mother is unwell, the children may be aware that something is wrong, and may feel deprived of attention and tenderness - a problem that can increase as the condition becomes more severe;
  c) **At work**: women with vulvodynia report increased loss of working days, as well as increased difficulties in concentrating or even staying seated at their desk. Many women go part time or leave their jobs, and can feel forced out of work.

Conclusions

Vulvodynia is a highly prevalent and serious condition that deserves to be diagnosed and cured **in order** to reduce the suffering of both women and their partners; to avoid progressive worsening to chronicity and comorbidities; to reduce personal, family and social costs; and to return women and their partners to a happier personal and intimate life. Vulvodynia is a legitimate medical entity, with a challenging spectrum of etiologies and clinical presentations, that deserves a rigorous, comprehensive and multidisciplinary approach.

Vulvodynia and Dyspareunia – How Should they be Addressed? 3

Vulvodynia (vulvar pain) and dyspareunia (painful intercourse) are closely related for anatomic, functional, pathophysiologic, emotional and relational reasons. Definitions of dyspareunia and vaginismus, also named 'sexual pain disorders' have varied in the past years.

Box 1. Definition of Dyspareunia and Vaginismus

- **Dyspareunia is defined as** persistent or recurrent pain with attempted or complete vaginal entry and/or penile vaginal intercourse.
- **Vaginismus** is defined as persistent or recurrent difficulties on the part of the woman in allowing 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/experience of pain, along with variable involuntary pelvic-muscle contraction. Structural or other physical abnormalities must be ruled out/addressed.
- **The disorder may be:**
  - lifelong vs acquired;
  - generalized vs contextual (i.e., limited to a specific partner and/or situation);
  - biological, psychogenic, or mixed.

The disorder may or may not cause personal distress. In the vast majority of cases, however, coital pain is a powerful trigger of personal and relational distress.

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Vulvodynia can trigger dyspareunia, and painful sexual intercourse may worsen or precipitate vulvar pain and help to maintain it (Fig. 3.1). The only exception is vulvodynia in children or virgin adolescents, or in women of any age who do not have penetrative sex.

A lifelong hyperactive pelvic floor ('myogenic hyperactivity', which may or may not be associated with phobia of penetration) anatomically reduces the size of the entrance of the vagina. This predisposes the introital vestibular mucosa to microabrasions resulting from the mechanical damage that can occur due to an attempt at sexual intercourse. A contributing factor is inadequate genital arousal, due to the reflex inhibition that pain and/or fear of pain (whether lifelong or acquired) has on vaginal lubrication and vulvar congestion. Mechanical mucosal damage immediately activates the mast cell response: when attempts at intercourse are recurrent, and/or coital damage persistent, and/or if concomitant factors such as a *Candida* vaginitis further contribute to the inflammatory state, there can be three key consequences (also see Chapter 6):

1. Hyperproduction of inflammatory molecules and neurotrophins such as nerve growth factor (NGF) by mast cells, which induces:

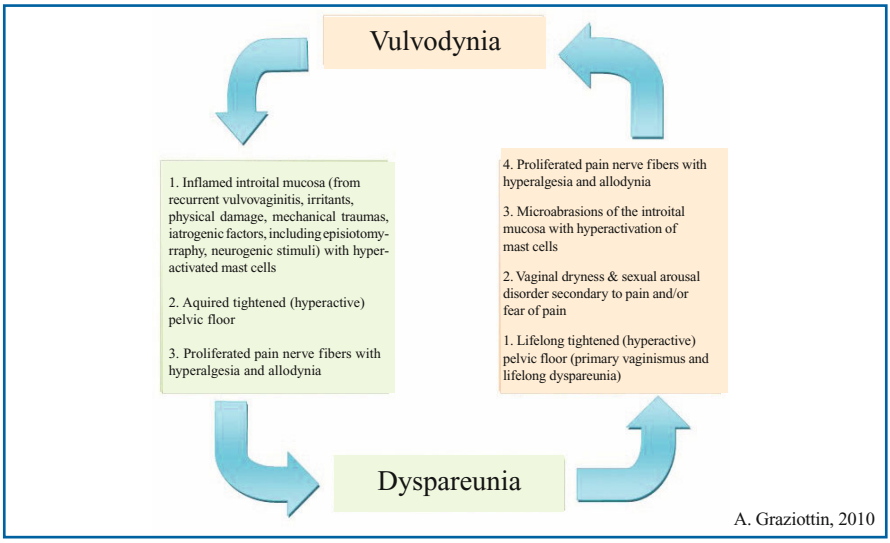

Fig. 3.1 Coital pain is associated to an inflammated introital mucosa, this for many causes. We can observe a defensive hyperactive pelvic floor (myogenic hyperactivity) followed by the proliferation of pain nerve fibers with hyperalgesia and allodynia. When, on a normal vestibular mucosa, the initial symptom is coital pain, the first consequence is the defensive contraction of the levator ani (like in primary vaginismus and lifelong dyspareunia). This predisposes the introital vestibular mucosa to microabrasions resulting from the mechanical damage that can occur due to an attempt at sexual intercourse, with hyperactivation of mast cells and finally a proliferation of pain nerve fibers and vulvodynia

2. proliferation of the pain nerve fibers responsible for introital hyperalgesia and allodynia, which in turn induces or worsens:
3. hyperactivity of the pelvic floor.

This is a vicious circle that can also work in reverse: beginning with recurrent/chronic inflammation of the introital mucosa, caused by infection (e.g., from *Candida*, *Herpes*, *Gardnerella*), physical damage (laser therapy or diathermocoagulation), chemical irritation (from soaps, perfumes, douche gel or other substances), allergies, iatrogenic insults (episiotomy-rraphy, or any other perineal surgery such as the removal of a Bartholin's cysts), life styles, such as the wearing of tight jeans, or neurogenic stimuli. These can induce the hyperactivation of the mast cell response, defensive contraction of the elevator ani (Fig. 3.2) and proliferation of pain nerve fibers via NGF.

Over time, a close reciprocity between vulvodynia and dyspareunia comes into play. In more serious cases this induces the progression of vulvodynia from provoked (by any genital or sexual stimulus or gynecologic examination) to unprovoked, from localized to generalized (with progressive comorbidity with bladder symptoms), and from dyspareunia to acquired loss of desire, arousal difficulties (mental and genital), orgasmic difficulties, and progressive avoidance of intercourse (Fig. 3.3). This has important consequences for the woman and her partner as it impacts direct-

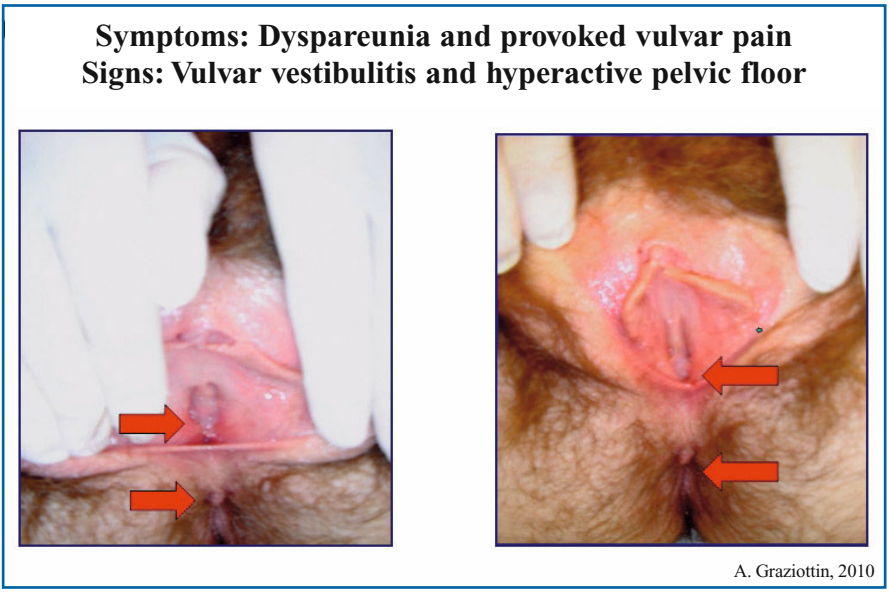

Fig. 3.2 Symptoms and signs may be correlated by listening carefully to the woman and performing an accurate clinical examination

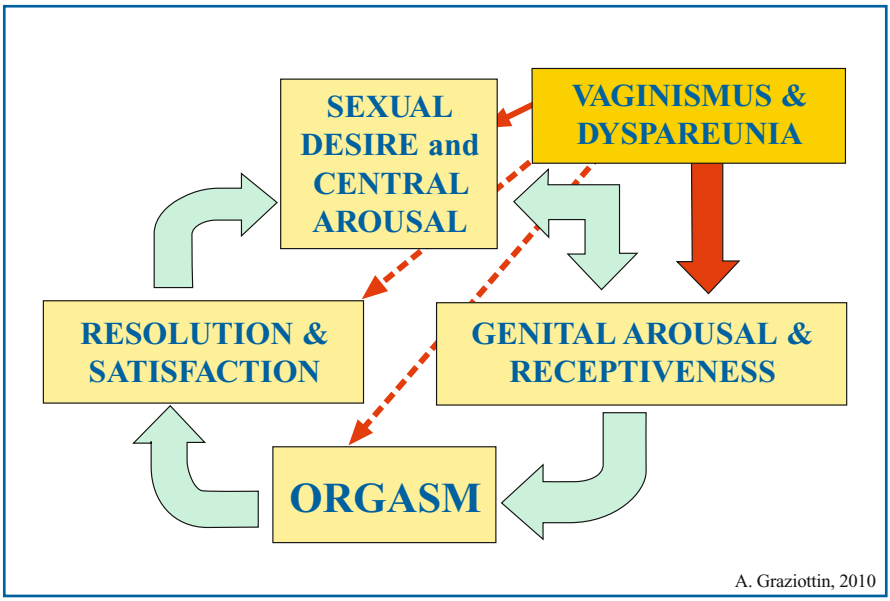

Fig. 3.3 Female Sexual Dysfunction (*FSD*) and dyspareunia. Coital pain (either due to vaginismus or other factors causing dyspareunia) directly inhibits vaginal lubrication, causing difficulties with genital arousal, vaginal dryness, orgasmic difficulties at intercourse, frustration, and dissatisfaction, and progressive avoidance of sexual intimacy in the majority of couples

ly on their intimate physical and emotional relationship (see Chapter 5 for more details).

Addressing Sexual Issues in the Clinical Setting

Despite the close relationship between vulvodynia and dyspareunia, physicians feel generally uncomfortable in investigating the sexual side of vulvodynia. This may be due to lack of training, fear of opening a Pandora's box of complaints and concerns, lack of time, or worries about being perceived as acting inappropriately or invasively by asking about sex.

Consequently, only a small minority of physicians routinely ask about coital pain while investigating vulvar pain-related complaints. And even fewer recommend abstinence from intercourse until the goal of complete healing of the introital mucosa, adequate relaxation of the pelvic floor and complete disappearance of vulvar pain has been achieved. Continuation of

sexual intercourse, a causative, predisposing, precipitating and maintining factor for dyspareunia and vulvodynia, contributes to the chronicity of pain and the shift between nociceptive and neuropathic pain. Other forms of sexual intimacy, such as foreplay, reciprocal masturbation or 'outercourse' may be enjoyed, however, at least in the less severe cases of vulvodynia.

Yet, there are key questions about sexual pain that must be asked if the significance and pathophysiology of vulvodynia are to be fully understood. When investigating the sexual side of vulvodynia, key recommendations include:

- raise the issue of sexuality when a general history is taken from the patient, beginning with a single, open-ended question, such as: "How's your sexual life?" or, simply: "Do you feel pain during intercourse or do you have other sexual difficulties?" This demonstrates to the patient that the physician is comfortable with the issue and sees it as an important aspect of his or her health and well being, avoiding the 'collusion of silence' that can occur if the patient is too shy or reserved to discuss the topic, and the physician too concerned to raise the issue;
- take seriously any sexual concern, regardless of the patient's age or medical status;
- be sensitive to gender and cultural factors, but do not make assumptions based on gender or cultural stereotypes when discussing sexual issues. Assume that every patient has his or her unique sexual history and needs;
- consider the role of the partner (if any) in the sexual relationship, and in any intervention keep an open mind about the dynamics of the couple's relationship;
- devote special attention to confidentiality, informed consent, and consider the potential limits of confidentiality, such as in the reporting of sexual abuse, especially in younger patients;
- avoid emotionally loaded terms, such as "sexual abuse". For example, ask the patient: "Have you ever had an unwanted sexual experience?" rather than, "Have you ever been sexually abused?". This approach is much more likely to elicit such information. A patient may say, for example: "I was drunk the first time I had sex and have felt guilty about it ever since," or, "I have had genital pain ever since", thereby suggesting important psychosexual co-factors in the etiology and persistence of pain;
- last but not least, be aware of your own areas of comfort and discomfort when addressing sensitive sexual issues (Tables 3.1 and 3.2).

Table 3.1 The scenario for addressing sexual issues (modified from Plaut M et al., 2004)

a) A proactive, empathic approach to your patient's sexual life will convey an attitude of availability and acceptance. Sexual issues may be discussed in a number of contexts, including:
   - obtaining background information about sexual function;
   - addressing possible consequences of illness, injury, procedure, or medication and specifically the potential comorbidity between vulvodynia and dyspareunia;
   - the presentation by the patient of a sexual problem or question.

b) It takes courage to disclose a sexual dysfunction or a sexual trauma. Such disclosures should be taken seriously and addressed in a sensitive manner.

c) Patients may reflect a wide diversity of experiences, values, and preferences:
   - all people may have sexual interests or concerns, including the elderly, the disabled, and those with chronic illness, such as vulvodynia and other types of chronic pain;
   - be sensitive to gender and cultural differences, but do not assume that any one patient necessarily fits a gender or cultural stereotype;
   - whenever possible, involve both the symptomatic patient and the partner in evaluation and treatment.

Table 3.2 Talking with patients about sexual issues (modified from Plaut M et al., 2004)

- 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, surprise, concern or pain;
- be sensitive to the impact of emotionally charged words (e.g. abortion, masturbation, rape);
- if you are not sure of the patient's sexual orientation, use gender neutral language in referring to his or her partner;
- explain and justify your questions and procedures;
- teach and reassure as you examine, specifically explaining every step when making the physical examination and describing the pain map in vulvodynia patients;
- intervene to the extent that you are qualified and comfortable; refer to qualified medical or mental health specialists as necessary.

Vaginismus and Dyspareunia: How Can they Contribute to Vulvodynia?

Although there is a longstanding tradition of distinguishing female sexual pain disorders into vaginismus and (superficial) dyspareunia, recent

research has demonstrated persistent problems with the sensitivity and specificity of the differential diagnosis of these two phenomena.

Both complaints may comprise, to a smaller or larger extent:

a. **Problems with muscle tension**: voluntary, involuntary, limited to vaginal sphincter, the bulbocavernous muscle, or extending to the pelvic floor, adductor muscles, back, jaws or entire body;
b. **Pain upon genital touching**: superficially located at the vaginal entry, the vulvar vestibulum and/or the perineum; either event-related (to the duration of genital touching/pressure), or more chronic (lasting for minutes/hours/days after termination of touching); ranging from unique association with genital touching during sexual activity to more general association with all types of vulvar/vaginal/pelvic pressure (e.g., sitting, riding a horse or bicycle, wearing tight trousers);
c. **Fear of sexual pain**: either specifically associated with genital touching/intercourse or more generalized fear of pain, or fear of sex;
d. **Propensity for behavioral approach or avoidance**: despite painful experiences with genital touching/intercourse, a subgroup of women continues to be receptive to sexual interaction initiated by a partner or by themselves. This continuation of sexual interaction may have very different psychodynamic meanings. Whether a conscious or unconscious choice, it may help to maintain closer bonding but at the price of worsening mucosal inflammation. On the other hand it may be perceived as frank abuse if it is imposed by the partner. The majority of patients affected by dyspareunia and/or vulvodynia tend, however, to progressively avoid intercourse.

In summary, mild lifelong hyperactivity of the levator ani and other muscles of the pelvic floor, which may coincide with grade I or II vaginismus (according to Lamont, Table 3.3), may permit intercourse while causing coital pain, thus contributing to lifelong dyspareunia. Severe hyperactivity of the levator ani, with variable phobia of penetration, is defined as severe vaginismus: it prevents intercourse and is the most frequent cause of unconsummated relationship or marriage in women. However, as no consensus has been reached so far in unifying the two entities, they will be kept separate according to the latest classification.

Table 3.3 Degree of vaginismus, evaluated in a gynecological setting (grades). Modified from Lamont JA, 1978, with permission

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

Pathophysiology

Vaginal receptiveness is a prerequisite for intercourse, and requires anatomic and functional tissue integrity, both in resting and aroused states. The necessary biologic conditions to guarantee vaginal 'habitability' are shown in Table 3.4. Vaginal receptiveness may be further modulated by psychosexual, mental and interpersonal factors, all of which may result in poor arousal with vaginal dryness.

Table 3.4 Biological factors contributing to maintain vaginal 'habitability'

- Normal trophism, i.e., healthy introital mucosa and vulvar skin;
- adequate hormonal impregnation, with estrogen (vaginal) and testosterone (vulva);
- normal tonicity of the perivaginal muscles, levator ani first;
- vascular, connective and neurological integrity;
- normal local immune response;
- no signs or symptoms of inflammation, particularly at the introitus.

Fear of penetration, and a general muscular arousal secondary to anxiety, may cause a defensive contraction of the perivaginal muscles, leading to lifelong vaginismus. This disorder may also be the clinical correlate of a primary neurodystonia of the pelvic floor, as recently demonstrated with needle electromyography. It may be so severe as to prevent penetration completely. Vaginismus is the leading cause of unconsummated marriages or relationships in women. Comorbidity between lifelong vaginismus and dyspareunia (see Fig. 3.1), and other female sexual dysfunction, is frequently reported. The defensive pelvic floor contraction may also be secondary to genital pain, of whatever cause.
Dyspareunia is the common symptom of a variety of coital pain-causing disorders (Table 3.5). Vulvar vestibulitis (VV), a subset of vulvodynia, is its leading cause in women of fertile age. The diagnostic triad is: 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) dyspareunia (see Chapter 6). Painful outcomes of episiotomy-rraphy and/or vulvar/perineal tears are the second (and neglected) cause of dyspareunia during the puerperium (see Capter 4).

Table 3.5 Etiology of dyspareunia: different causes may overlap, with complex and dynamic pathophysiologic interplay (adapted from Graziottin A, 2005)

A) Biological

1) Superficial/introital and/or mid-vaginal dyspareunia

- infectious: vulvitis, vulvar vestibulitis, vaginitis, cystitis;
- inflammatory: with mast cell up-regulation;
- hormonal: vulvo-vaginal atrophy;
- anatomical: fibrous hymen, vaginal agenesis, Rokitansky syndrome;
- muscular: primary or secondary hyperactivity of levator ani muscle;
- iatrogenic: poor outcome of genital or perineal surgery; pelvic radiotherapy;
- neurologic, inclusive of neuropathic pain;
- connective and immunitary: Sjogren's syndrome;
- vascular;
- female genital mutilation, with introital/vaginal narrowing.

2) Deep dyspareunia

- endometriosis;
- Pelvic Inflammatory Disease (PID);
- chronic pelvic pain and referred pain;
- pelvic varicocele;
- outcome of pelvic radical surgery or endovaginal radiotherapy;
- Abdominal Cutaneous Nerve Entrapment Syndrome (ACNES).

B) Psychosexual

- comorbidity with desire and/or arousal disorders, or vaginismus;
- past sexual harassment and/or abuse;
- affective disorders: depression and anxiety;
- catastrophism as leading psychological coping modality.

C) Context or couple related

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

Clinical Approach: Taking a Clinical History

In sexual pain disorders, an accurate clinical history and careful physical examination are essential for ascertaining a diagnosis and a prognosis. The location

and characteristics of pain have been demonstrated to be the most significant predictors of its etiology. No instrumental exam has so far been demonstrated to be more informative than a carefully performed clinical examination.

Focusing on the presenting symptom - dyspareunia - and with the above-mentioned attention to the sensitivity of the issue, the key questions required to obtain the most relevant information can be summarized as follows:

- Did you experience coital pain from the very beginning of your sexual life onwards (lifelong) or did you experience it after a period of normal (painless) sexual intercourse (acquired disorder)?

- (If lifelong) Were you afraid of feeling pain before your first intercourse?

Key point: When lifelong, dyspareunia is usually caused by mild/moderate vaginismus (which causes painful penetration) and/or coexisting, life-long low libido and arousal disorders.

- (If acquired) Do you remember the situation or what happened when it started?

Key point: The answer can give information about the "natural history" of the current sexual complaint, and the "personal reading" the woman has of her problem, of significant co-factors and meaning.

- Where does it hurt? At the beginning of the vagina, in the mid vagina or deep in the vagina?

Key point: The location of pain and its onset within an episode of intercourse is the strongest predictor of presence and type of organicity.

– introital dyspareunia may be more frequently caused by poor arousal, mild vaginismus, vulvar vestibulitis, vulvar dystrophia, painful outcome of vulvar physical therapies, perineal surgery (episiorraphy, colporraphy, posterior perineorraphy), female genital mutilation with introital/vaginal narrowing, pudendal nerve entrapment syndrome and/or pudendal neuralgia, Sjogren's syndrome;

– mid-vaginal pain, acutely evoked during physical examination by a gentle pressure on the sacro-spinous insertion of the levator ani muscle, is more frequently due to levator ani myalgia, the most frequently overlooked biological cause of dyspareunia;
– deep vaginal pain may be caused more frequently by endometriosis, chronic pelvic pain or pelvic inflammatory disease (PID) or by outcomes of pelvic radiotherapy or vaginal radical surgery. Varicocele, adhesions, referred abdominal pain, and abdominal cutaneous nerve entrapment syndrome (ACNES) are less frequent and still controversial causes of deep dyspareunia, which should nevertheless be considered in the differential diagnosis.

• When do you feel pain? Before, during or after intercourse?

Key point: the timing of pain with respect to intercourse is critical in understanding the cascade of pathophysiologic events, the potential relationship between vaginismus and dyspareunia and leading comorbidities.

– pain before intercourse suggests a phobic attitude towards penetration, usually associated with vaginismus, and/or the presence of chronic vulvar vestibulitis, clitoralgia and/or vulvodynia, which may also facilitate pain in the arousal state during foreplay and before penetration;
– pain during intercourse is more frequently reported. This information, combined with the previous question, “Where does it hurt?”, is the most predictive of the organicity of pain;
– pain after intercourse indicates that mucosal damage was provoked during intercourse, possibly because of poor lubrication, leading to vestibulitis, pain and defensive contraction of the pelvic floor.

• Do you feel other accompanying symptoms, vaginal dryness, pain or abnormal sensation in the genitals and pelvic areas? Or do you suffer from cystitis 24-72 hours after intercourse?

Key point: attention to accompanying symptoms is key for the early diagnosis of comorbidities and appropriate understanding of the pathophysiology of the current complaint(s).

– vaginal dryness, either secondary to loss of estrogen and/or to poor genital arousal may coincide with/contribute to dyspareunia;

– clitoralgia and/or vulvodynia, spontaneous and/or worsening during sexual arousal may be associated with dyspareunia, hypertonic pelvic floor muscles, and or neurogenic pain, inclusive of pudendal nerve entrapment syndrome;
– post-coital cystitis should suggest a hypoestrogenic condition and/or the presence of hypertonic pelvic floor muscles: it should specifically be investigated in young women complaining of 'burning bladder' symptoms (and syndrome) in comorbidity with dyspareunia; and in post-menopausal women who may benefit from topical estrogen treatment and rehabilitation of the pelvic floor, aimed at relaxing the myalgic perivaginal muscles;
– vulvar pruritus, vulvar dryness and/or feeling of a burning vulva should be investigated, as they may suggest the presence of vulvar lichen sclerosus, which may worsen introital dyspareunia. Neurogenic pain may cause not only dyspareunia but also clitoralgia. Eye and mouth dryness, when accompanying dyspareunia and vaginal dryness, should suggest Sjogren's syndrome.

- How intense is the pain you feel?

Key point: Focusing on the intensity and characteristics of pain is relatively new approach in addressing dyspareunia. A shift from nociceptic to neuropathic pain is typical of chronic dyspareunia, and treatment may require a systemic and local analgesic approach.

Practical Tips

Suggest patient keeps a *diary of pain*, mirroring the menstrual cycle phases if the woman is in her fertile age (i.e., starting every page with the first day of her cycle, with the date on the x axis, and the 24 hours of the day in the y axis. Pain intensity could be reported with three colours: zero pain = white; 1 to 3 = yellow; 4 to 7 = red; 8 to 10 (worst pain ever) = black).

This will: 1) improve the recording and understanding of pain flares before, during and/or after the menstrual cycle, and the circadian rhythm of pain, to improve the diagnosis, etiology and contributors of pain; 2) suggest a better way to tailor the analgesic treatment; 3) make more accurate the recording of the impact of treatment on pain perception. Typically, nociceptive pain persists and worsens at night, while neuropathic pain is significantly reduced or absent during sleep.

Conclusions

Pain is rarely purely psychogenic, and dyspareunia is no exception. Like all pain syndromes, it usually has one or more biologic etiologic origins. Hyperactive pelvic floor disorders are a constant feature and comorbidity with urologic and/or proctologic disorders is a frequent and yet neglected area to be explored for comprehensive treatment.

Psychosexual and relationship factors, generally lifelong or acquired low sexual desire because of persistent pain, and lifelong or acquired arousal disorders due to the inhibitory effect of pain, should be addressed in parallel, in order to provide comprehensive, integrated and effective treatment.

Vaginismus, which may contribute to lifelong dyspareunia, when mild/moderate, and may prevent intercourse, when severe, needs to be better understood in its complex neurobiologic, muscular and psychosexual etiology, and addressed via a multimodal approach.

In patients with vaginismus, the diagnosis and prognosis may be made based on three variables:

- intensity of phobic attitude (mild, moderate, severe) toward penetration;
- intensity of pelvic floor hypertonicity (in four degrees, according to Lamont);
- co-existing personal and/or relational psychosexual problems.

Relationship issues should be diagnosed and appropriate referral considered when the male partner presents with a concomitant male sexual disorder.

Postpartum Dyspareunia and Vulvodynia 4

Vulvodynia is often sadly neglected after delivery, despite its frequent comorbidity with dyspareunia in this vulnerable phase of a woman's life. Although it is not the only sexual complaint occurring after delivery, dyspareunia is a problem that requires specific medical/gynecological attention to its biological basis, as well as careful evaluation of the delivery outcome and the condition of the pelvic floor.

The prevalence of female sexual dysfunction (FSD) is high after childbirth, in the postpartum and puerperium periods. Data indicate that up to 86% of women report one or more FSD soon after delivery. The most frequently reported complaint is low libido, which is more prevalent in women who are breastfeeding (because, in addition to inducing amenorrhea, high prolactin has a negative impact on the neurobiological basis of sexual drive).

The Prevalence of Postpartum Dyspareunia

Dyspareunia and vaginal dryness frequently occur after childbirth, and may independently contribute to a reduction in sexual drive, because of the negative feedback from the genitals. One study showed that at 6 months post partum about one-quarter of all primiparous women reported reduced sexual sensation, worsened sexual satisfaction, and reduced ability to achieve orgasm, as compared with the period before they gave birth. At 3 and 6 months post partum, 41% and 22% respectively reported dyspareunia.

Relative to women with an intact perineum, those with second-degree perineal trauma were 80% more likely (95% confidence interval [CI]

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1.2–2.8) and those with third- or fourth-degree perineal trauma were 270% more likely (95% CI 1.7–7.7) to report dyspareunia at 3 months post partum.

At 6 months post partum, the use of vacuum extraction or forceps was significantly associated with dyspareunia (odds ratio [OR] 2.5; 95% CI 1.3–4.8), and women who breastfed were ≥4 times as likely to report dyspareunia as those who did not breastfeed (OR 4.4; 95% CI 2.7–7.0). Episiotomy conferred the same "negative" profile of sexual outcomes as spontaneous perineal lacerations.

A variable percentage of women who report dyspareunia and consequent vulvodynia undergo a "shift" to spontaneous vulvar pain; if the complaint is not adequately and promptly addressed, this has a dramatic impact on a woman's life and on her marriage.

Persistent Morbidity and Lack of Professional Recognition

As Glazener pointed out in 1997, persistent morbidity and lack of professional recognition still mean that many women do not receive a prompt diagnosis and therapy for their dyspareunia/vulvodynia. This adds to the disruption of a woman's sexuality and the quality of sexual intimacy at a time when her relationship is already extremely vulnerable to the challenges and needs of the newborn.

Prevention of Postpartum Dyspareunia/Vulvodynia

It is very important for the clinician to focus on few, practical points and these are discussed next.

Accurate Pelvic Floor Training During Pregnancy

Midwifes are the healthcare providers that are best placed for, and trained in, teaching pregnant women a number of key steps of self-awareness and empowerment:

- knowledge of the pelvic floor, its muscles and their functions;
- increasing competence in responding to the command to contract and completely relax the pelvic floor, with appropriate breathing (yoga can help);
- learning a competent and efficient "pull strategy";

- in the case of a hyperactive pelvic floor (which is more frequently associated with lifelong dyspareunia and/or vulvodynia), it is essential to use "hands-on" training to teach the woman to relax the pelvic floor, using more specific physiotherapy techniques such as pelvic floor stretching and perineal work.

Key point: The goal is to empower the woman to deliver with an improved body image; a competent dynamic perception of the pelvic floor; and appropriate self-confidence in her ability to properly command her muscles, breathing slowly, deeply and appropriately, and behaving as the true protagonist of a well carried out vaginal delivery.

Antepartum instruction on how to perform pelvic floor exercises is important: in contrast to women who performed pelvic floor exercises, women who were not instructed did not regain antepartum pelvic floor contraction pressures 8 weeks after vaginal delivery and complained of more vulvar pain and dyspareunia.

Adequate Assistance at the Second Stage of Labor

Assistance is invaluable in the second stage of labor, when the baby's head emerges and distends the pelvic floor. Appropriate and timely pelvic floor massage, performed "hands-on" by the assisting midwife, may ease the baby's passage, supporting the pelvic floor, and reducing the risk of pudendal nerve damage during delivery and the risk of perineal and clinically visible anal sphincter tears, which are reported in up to 6.4% of vaginal deliveries. Occult sphincter defects occur in up to 33% of primiparous and 4% of multiparous women after vaginal delivery. Direct perineal assistance by the midwife, if started before the second stage of labor begins, may contribute to improving the pelvic floor stretching, thus easing the head passage, while giving the woman a definite and reassuring sense of being individually well cared for.

- **Position for birth**: a systematic Cochrane database review concluded that the adoption of any upright or lateral position for birth is associated with a shorter second stage of labor, protects the perineum, and is associated with fewer instrumental deliveries and fewer episiotomies.
- **Limit episiotomy to selected cases**: systematic reviews of episiotomy for vaginal birth concluded that restrictive use of episiotomy is superior to routine episiotomy in relation to perineal trauma, suturing, healing, and dyspareunia. Specifically, perineal pain, disturbed wound healing,

and dyspareunia are more common in women who have delivered with a mediolateral episiotomy than with a midline episiotomy or with spontaneous perineal tears. Women in the group with restricted use of episiotomy and those with an intact perineum started postpartum sexual intercourse earlier than women in a group that underwent routine episiotomy. Overall, sphincter laceration is more frequent when midline episiotomy is performed. Vacuum extraction and forceps delivery may specifically contribute to damaging the pelvic floor, causing pudendal nerve damage and vulvodynia – either spontaneous or provoked by intercourse. Epidural anesthesia/analgesia for vaginal delivery is associated with a higher incidence of instrumental deliveries, which may increase the occurrence of episiotomy and subsequent dyspareunia. Pudendal nerve damage during delivery may variably contribute to FSD, and specifically vulvodynia, after childbirth. However, to the authors' knowledge, there are no accurate figures available on this potential contributor to postpartum vulvodynia.

The primary question is whether or not to use an episiotomy routinely.

Increasing evidence supports the restrictive use of episiotomy compared with its routine use.

- **Accurate suturing of the episiotomy**: episiorrhaphy is a simple but not insignificant medical procedure. When it is not adequately performed, with no respect for the appropriate reconstruction of different tissues and planes, or when rigorous asepsis is not respected, infection and local abscesses may dramatically increase the risk of a retracting scar, painful introital trigger points, or dyspareunia and vulvodynia.

Key point: Adoption of an upright birth position, perineal massage, warm compresses to the perineum to relax the elevator ani, and flexion of and couterpressure to the baby's head may reduce both episiotomies and sphincter lacerations. Overall, the restrictive use of episiotomy is superior to routine episiotomy, with respect to perineal trauma, suturing, healing, and dyspareunia.

Postpartum Therapy

The following *medical interventions* may be used postpartum:

- appropriate care of the episiorrhaphy;
- careful vulvar hygiene. An Italian multicenter study has shown that personal genital hygiene with thymus extracts after childbirth significantly reduces dyspareunia and vaginal dryness, while also increasing sexual desire, genital arousal, and orgasm. Reduction of negative feedbacks from the genitals, because of the reduction of dyspareunia and vulvodynia, may explain the increase in desire, arousal, and orgasm;
- the woman herself may perform vaginal stretching and massage for a few minutes, two to three times a day, to prevent retracting/painful scars and to promote better tissue elasticity;
- local estrogens: estradiol, estriol, or promestriene, twice a week, are minimally absorbed (<1%). They can be used on medical prescription, and contribute to reducing the vaginal pH, improving the vaginal ecosystem, and easing vaginal lubrication, thus reducing vaginal dryness and dyspareunia;
- appropriate treatment of constipation, which usually worsens in pregnancy, and may contribute to vaginitis and cystitis from infection with *E. coli*, *Enterococcus faecalis* etc.

Psychosexual intervention may be indicated for:

- *women* who complain of postpartum depression, traumatic delivery with or without post-traumatic stress disorder, difficulty in regaining a positive body image, or persisting loss of sexual desire, and also after successful treatment of vaginal dryness, dyspareunia, spontaneous or provoked vulvodynia;
- *couples*: when conflicts, jealousy, or other difficulties make it more difficult to regain a satisfying sexual and emotional intimacy, contributing to low desire, and arousal difficulties with vaginal dryness, dyspareunia, and coital anorgasmia.

Key point: Early recognition of postpartum dyspareunia, and adequate diagnosis and treatment of the different potential contributory factors, may significantly reduce postpartum coital pain and consequent vulvodynia. It may also reduce the number of women whose pain, if persistently unaddressed and untreated, may shift from being nociceptive to becoming neuropathic, contributing to spontaneous vulvodynia.

What Women with Vulvodynia Complain of: Evaluation of Vulvar Pain

5

"I've had pain and burning near the entrance to my vagina for a long time. My doctor says it's probably vulvodynia".

What do women with vulvodynia complain of? There are two key issues: pain at intercourse and/or vulvar pain.

Pain is emotionally detrimental and consciously avoided. However, it is absolutely crucial for our survival. Pain perception is one of the most complicated measurable traits because it is an aggregate of several phenotypes associated with peripheral and central nervous system dynamics, responsiveness to stress and inflammatory state.

Vulvodynia is defined as chronic *vulvar pain* in the absence of objective clinical or laboratory findings to explain the symptoms. Itching is absent or is a minor symptom that does not produce a need to scratch.

Nevertheless, a good working definition for vulvodynia is a vulvar condition where the dominant symptom is a *variation on the pain theme*.

Box 1. Vulvar pain

- Vulvar pain is often described as having a burning quality
- Other patients describe their problem as "irritation", "stinging", "raw feelings", "crawling", or just "vulvar awareness"
- Discomfort has also been referred to as "the pain down there" or as "feminine pain"
- Vulvar pain can be:
  - provoked: it occurs in response to stimulation
  - unprovoked: it occurs independently of stimulation

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Dyspareunia is genital pain experienced just before, during or after sexual intercourse. Patients with dyspareunia may complain of a well-defined and localized pain, or express a general disinterest in and dissatisfaction with intercourse that stems from the associated discomfort. The most common pain with dyspareunia occurs during coitus, but some women experience pain afterwards, while others report pain at both times. Pain before coitus may result from irritation of the external genitalia or the vasocongestion that occurs during the excitement phase. Patients with dyspareunia are more likely than the general population to report pain with insertion of a tampon or digit, or during a gynecologic examination.

Box 2. Marinoff Dyspareunia Scale

0	No dyspareunia
1	Causes discomfort but does not interfere with frequency of intercourse
2	Sometimes prevents intercourse
3	Completely prevents intercourse

Dyspareunia has been associated with a more negative attitude toward sexuality, with more sexual function impairment and with lower levels of relationship adjustment.

Women with dyspareunia, not surprisingly, have been found to have a lower frequency of intercourse and lower levels of desire and arousal, and to be less orgasmic with oral stimulation and intercourse. When tenderness is elicited during the examination, the physician can ascertain if this pain is similar to her dyspareunia.

There are two major pain patterns in women with vulvodynia: vestibulodynia (vulvar vestibulitis syndrome) or generalized vulvodynia. Vestibulodynia, the most frequent type of vulvodynia, is defined as burning or pain that is localized strictly to the vestibule of the vulva and is provoked by pressure or friction in the vestibule. Pain is commonly associated with intercourse, tampon use, tight clothes, and bicycle riding, among others, and spontaneous pain is minimal or absent.

The second pattern of vulvodynia is generalized vulvodynia, which is associated with burning or pain that is not limited to the vestibule and may occur without touch or pressure. When asked to localize this sort of pain, patients are frequently unable to do so, and are only able to indicate the general area where the pain is experienced.

Dyspareunia is an important component of vulvodynia and it can occur as an isolated symptom.

Dyspareunia is a component of vulvar pain related to the 'provocation' of sexual intercourse and it may be the only symptom, especially in provoked vestibulodynia.

The symptom of vulvar pain must be fully evaluated. As pain is subjective, the patient's history provides the main evaluation. Examination and investigations provide further understanding of the pain syndrome and exclude other conditions.

Box 3. Vulvar pain evaluation

- Baseline and ongoing regular evaluation of pain severity
- An initial detailed history to include: chronology of onset and progression, characteristics and site of pain, including radiation, aggravating and relieving factors, associated symptoms
- Questions about thoughts, emotions and behavior associated with pain
- Detailed examination, not only of the painful area but of the whole patient, particularly musculoskeletal and nervous systems

Vulvar pain can only be measured subjectively. The most reliable and well-understood method is a numerical rating scale, from 0 (no pain) to 10 (extreme pain), with half-points marked. This is superior to the widely used visual analogue scale (VAS), which is a 10-cm line with 'no pain' marked at one end, and 'extreme pain' at the other. Alternatively, a simple verbal rating scale can be used, e.g. 'none', 'mild', 'moderate', 'severe'. Both numerical and verbal scales can be used by patients without the need for paper and pen, unlike the VAS.

Because pain is multidimensional, a single rating scale combines these dimensions in unknown quantities. Depending on the clinical question, treatment, patient and setting, it can be helpful to assess separately pain intensity, pain distress, and interference of pain with activities of daily life. It can also be helpful to ask about average pain, worst pain (as even if this only occurs rarely, it can still reveal what patients should avoid) and pain on, for example, bladder voiding. Pain reduction or relief is measured directly using a percentage, from 0% = no relief up to 100% = total relief.

Classically, pain can be considered to have three dimensions: sensory-discriminative, motivational-affective and cognitive-evaluative. The most used and validated multidimensional tools for the measuring pain are the

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Short-Form McGill Pain Questionnaire – Ronald Melzack

Patient's name: Date:

Definition of pain	None	Mild	Moderate	Severe
Throbbing	0)	1)	2)	3) .....
Shooting	0)	1)	2)	3) .....
Stabbing	0)	1)	2)	3) .....
Sharp	0)	1)	2)	3) .....
Cramping	0)	1)	2)	3) .....
Gnawing	0)	1)	2)	3) .....
Not-burning	0)	1)	2)	3) .....
Aching	0)	1)	2)	3) .....
Heavy	0)	1)	2)	3) .....
Tender	0)	1)	2)	3) .....
Splitting	0)	1)	2)	3) .....
Tiring-exhausting	0)	1)	2)	3) .....
Sickening	0)	1)	2)	3) .....
Fearful	0)	1)	2)	3) .....
Punishing-cruel	0)	1)	2)	3) .....

Fig. 5.1 The Short Form McGill Pain Questionnaire (adapted from Melzack R, 1987, with permission)

long and short forms of the McGill Pain Questionnaire (Fig. 5.1). The questionnaire consists primarily of three major classes of word descriptors - sensory, affective and evaluative - that are used by patients to specify subjective pain experience. It also contains an intensity scale and other items to determine the properties of the pain experience. The questionnaire was designed to provide quantitative measures of clinical pain that can be treated statistically.

In conclusion, vulvar pain analysis and quantification is optimal for a comprehensive understanding of the patient's experience and for effective treatment planning. Pre- and post-treatment quantification of vulvar sensitivity can lead to advances in the optimization of treatment success.

How Vulvodynia Originates: the Pathophysiology of Vulvar Pain

6

Vulvodynia is a complex syndrome of vulvar pain with sexual dysfunction and psychological disability. Its etiology remains elusive but several lines of investigation support a neuropathic etiopathogenesis for the disease. The manifestation of vulvodynia may be caused by more than one factor and may vary in each patient.

Vulvar pain is an unpleasant and emotionally arousing sensory experience that invades womens' consciousness, and chronic pain is maladaptive and evokes human suffering. Chronic (also known as persistent) pain is defined when it last for at least 3 months. However, the mechanisms involved are more important than the duration of the pain. Chronic pain is associated with changes in the central nervous system (CNS), which may maintain the perception of pain in the absence of acute injury.

Recent evidence from human studies has significantly expanded the understanding of pain perception and has demonstrated that a complex series of spinal, midbrain, and cortical structures are involved in pain perception.

How Complex Is Vulvar Pain Transmission into the Central Nervous System?

Pain transmission from the periphery to the higher brain centers via the spinal cord is not a simple, passive process involving exclusive pathways (Fig. 6.1). The relationship between a stimulus causing pain and the way it is perceived by an individual is dramatically affected by circuitry within the spinal cord and the brain. The sensation of pain is modulated as it is transmitted upwards from the periphery to the cortex. It is modulated at a

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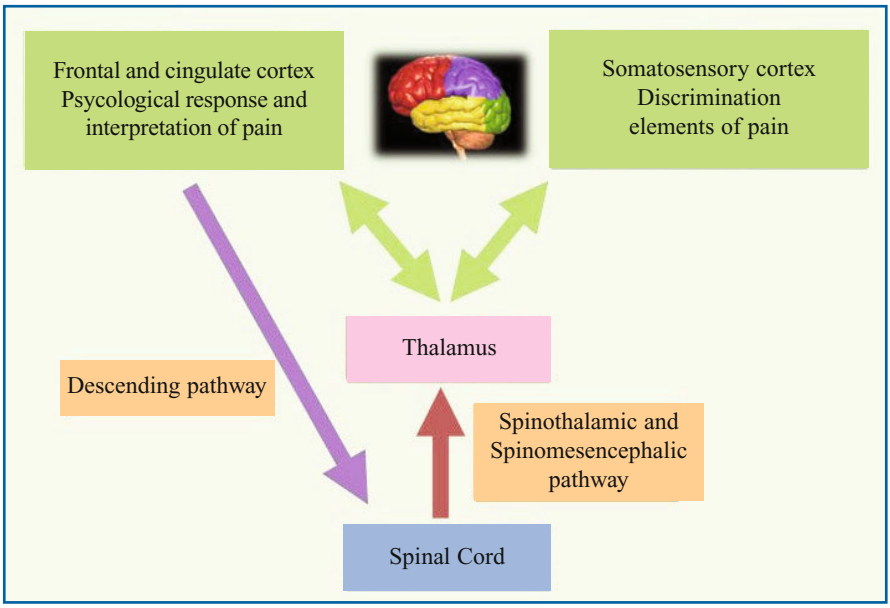

Fig. 6.1 Schematic representation of pain pathways

segmental level and by descending control from higher centers, with the main neurotransmitters involved being serotonin, norepinephrine (noradrenaline) and the endogenous opioids.

- **The peripheral nociceptors** are simple bare-ending nerve fibers that are wide-spread in the superficial layers of the skin. Nociceptors are classified as: Aδ, which are small-diameter, lightly myelinated, and C-fibres, which are not myelinated. Neurons originating at the nociceptors pass into the peripheral nerves and enter the spinal cord at the dermatomal level ascribed by their insertion. Innervation to the vulva is via the pudendal nerve which originates from the S2–4 nerve roots and the ilioinguinal and genitofemoral nerves, arising from L1–2. The latter two nerves are predominantly sensory, but the pudendal nerve contains motor, sensory, and sympathetic fibers which supply the complex autonomic reflexes of the pelvic organs. The vagina itself is relatively insensitive to pain, while the vulva and particularly the vulvar vestibule have a high level of free nerve endings.
- **Spinal cord**. Following spinal-cord integration of afferent inputs there are neurons (second-order neurons) that transmit the information to the higher centers via ascending pathways. The classical ascending pathway ascribed to pain is the spinothalamic one; other pathways relevant in pain modulation include the spinomesencephalic, spinoreticular and dorsal column pathways.

- **Cerebral cortex**. Cortical pain perception can be roughly divided into a lateral, somatosensory system involved in the discrimination of pain location and intensity, and a medial system which mediates the anticipatory, fearful, affective quality of pain through limbic structures. In broad terms, pain has elements that are sensory and localizing, and other elements that are involved in memory, cognition and affect.
- **Descending pathways**. Some of the spinothalamic fibers project to the periaqueductal grey (PAG) and hypothalamus and then to the dorsal horn of the spinal cord. The PAG is an area of the brain that is rich in opioid receptors and is thus involved in the endogenous opioid system. The descending pathways are, therefore, inhibitory at the dorsal horn, reducing ascending nociceptive inputs.

What Happens in Neuropathic Pain and why Can We Consider Vulvodynia as a Neuropathic Pain Syndrome?

Neuropathic pain is defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Neuropathic pain results from damage to the nervous system anywhere along the neuraxis: peripheral nervous system, spinal or supraspinal nervous system, or brain. Clinically, neuropathic pain is expressed by two abnormal sensory processes manifest as *hyperalgesia* and/or *allodynia*. Hyperalgesia is defined as an increased response to a stimulus that is normally painful, while allodynia as pain due to a stimulus that is not normally painful.

Vulvodynia patients exhibit these two basilar elements: hyperalgesia and/or allodynia.

Box 1. Glossary

- **Allodynia**: Pain perception evoked by a stimulus that under normal conditions evokes non-painful sensations
- **Central sensitization**: A phenotypic change in CNS pathways that leads to the augmentation of the processing of nociceptive stimuli
- **Hyperalgesia**: Enhanced pain perception evoked by a stimulus that under normal conditions evokes painful sensations
- **Nociception**: Pain and pain behaviors evoked by the application of a brief noxious stimulus
- **Nociceptors**: Primary nerve fibers that respond to tissue injury or stimuli that are capable of evoking tissue injury

6

The steps involved in generation of neuropathic pain (Fig. 6.2) are:

- **Peripheral change after nerve damage**. Injury to free nerve endings induces structural and functional changes in both injured and uninjured parts of the nerve. These changes increase ectopic and spontaneous firing after nerve damage, furthermore 'cross-talk' from neighboring nerves (damaged or not) can augment this effect. Regeneration of axon terminals after nerve damage may enhance cross-talk, although the degree of sprouting does not correlate with the severity of pain behaviors. Hyperalgesia and allodynia are the symptomatic expressions of these phenomena. Inflammation has been suggested to be pivotal to the development of peripheral sensitization. Nerve grow factor (NGF) appear to be a key molecule in the orchestration of peripheral inflammation. NGF is released from many cells after tissue injury and has several pro-inflammatory roles. Indeed, NGF has significant action on the expression of other inflammatory mediators (interleukin-1ß and tumor

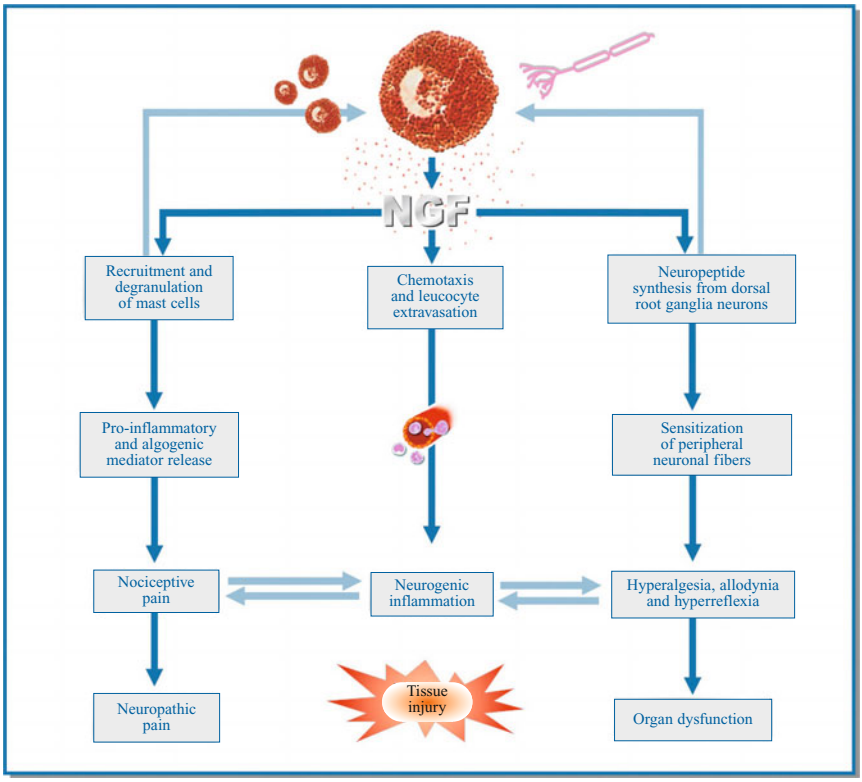

Fig. 6.2 Mast cell activation

necrosis factor, etc.) and it is also capable of direct and indirect sensitization of nociceptors. Inflammation-driven release of cytokines from immune cells provokes hyperalgesia through stimulation and production of other pro-inflammatory agents.

Mast cells are the main source of inflammatory mediators. These peripheral cell types are located in the dermis, adjacent to blood vessels, nerve endings and glandular ducts, and have a cytoplasm filled with spherical granules. Mast cell granules contain many factors implicated in neurogenic inflammation, such as NGF, tumor necrosis factor (TNF), proteases and cytokines.

Physical, chemical and mechanical stimuli activate local mast cells, causing degranulation and secretion of mediators that have been found to sensitize and induce the proliferation of C-afferent nerve fibers. These nerve fibers release inflammatory mediators, including NGF, which increase the proliferation and degranulation of mast cells, causing hyperesthesia, and enhance the inflammatory response. Mast cells show particular complexity in relation to the inflammatory response, and their density in inflamed tissue changes over time. In tissue where there is an acute inflammatory response, the concentration of mast cells is high. As the inflammation becomes more chronic the number of mast cells decreases and there is a parallel increase in neuronal proliferation. At this stage of the inflammatory process neuropathic symptoms became prominent, but mast cell reactivation can occur at any time, with an exacerbation of symptoms or acceleration of neurogenic inflammatory processes.

- **Central mechanism**. The dorsal horn is now known to play a key role in the modulation of pain (Fig. 6.3) and the development of chronic pain states. Pain is perceived only if this electrical activity reaches the brain and, hence, any modulation of alteration within the dorsal horn can have profound effects on pain sensation. Laminas IV and V of the dorsal horn contain a peculiar type of neuron called wide dynamic range (WDR). Repetitive stimulation by C-fibers cause some WDR cells in the dorsal horn to augment their response. Thus, for a given input stimulus, the output is enhanced; this process is referred to as ‘wind up’. Wind up is a part of a process termed ‘central sensitization’. Cortical functioning has localizing, emotional and memory components. Descending modulatory control is bidirectional in nature. These descending control systems link the brain cortex to the dorsal horn, acting either directly on primary afferents or indirectly via inhibitory and excitatory interneurones.

  The phenomena described above lead to central sensitization, a pivotal aspect of neuropathic pain. Central sensitization involves an increase in

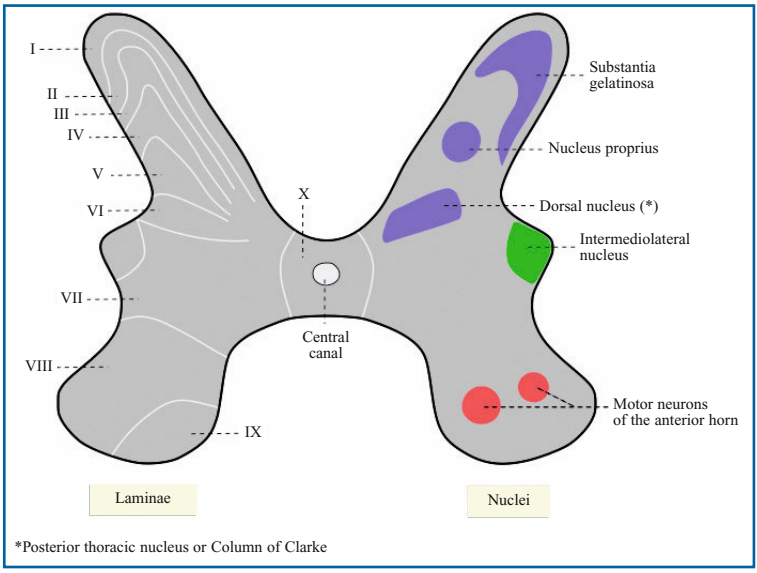

Fig. 6.3 Structure of the dorsal horn

the receptive fields of a nociceptor, an increase in the magnitude and duration of its response to a noxious stimulus and a reduction in the threshold required to stimulate nociceptors.

What happens in vestibulodynia/vulvodynia patients?

Vestibular proliferation of C-afferent receptors (ten-fold increase in the density of nerve endings) and a significant number of activated mast cells (assessed by measuring mast cell degranulation levels) have been reported in vestibulodynia patients.

Biopsies from the area around the ductal openings of Bartholin glands, the most sensitive vestibular area in most vestibulodynia patients, have shown significantly more intraepithelial free nerve endings than in healthy control subjects.

It is possible that the epithelium of the vulvar vestibule expresses an abnormal response to 'trigger' inflammatory events such as infection, trauma and repeated exposure to an irritant or allergen, with a subsequent increase in the number of activated mast cells. Their activation is associated with the discharge of various mediators from the granules, such as NGF, tryptase and bradykinin. The various mediators secreted by mast cells are

known to sensitize C-nerve fibers and induce their proliferation. *Neurogenic inflammation* is the most appropriate definition of this series of events (Fig. 6.4).

Recent lines of evidence highlight a potential genetic predisposition to chronic inflammation among vestibulodynia-afflicted women. These genetic polymorphisms lead to a reduced capacity to terminate and to an exaggerated inflammatory response.

The findings of multiple case-control studies of women with provoked vestibulodynia suggest that they experience more frequent vaginal infections. A history of recurrent candidiasis infections is one of the most consistently reported findings associated with the onset of vestibolodynia. A reduced capacity to control *Candida albicans* action due to a polymorphism in the gene coding for mannose-binding lectin, an innate immune system antimicrobial protein, has been reported and this polymorphism has also been associated with vestibulodynia.

It has also been demonstrated that women with vulvodynia more frequently react to patch tests for *Candida albicans*, and it was postulated that exposure to *Candida albicans* at low concentrations may involve neurotransmitters that have been shown to influence contact hypersensitivity and are present in abundance in the vulvar vestibule.

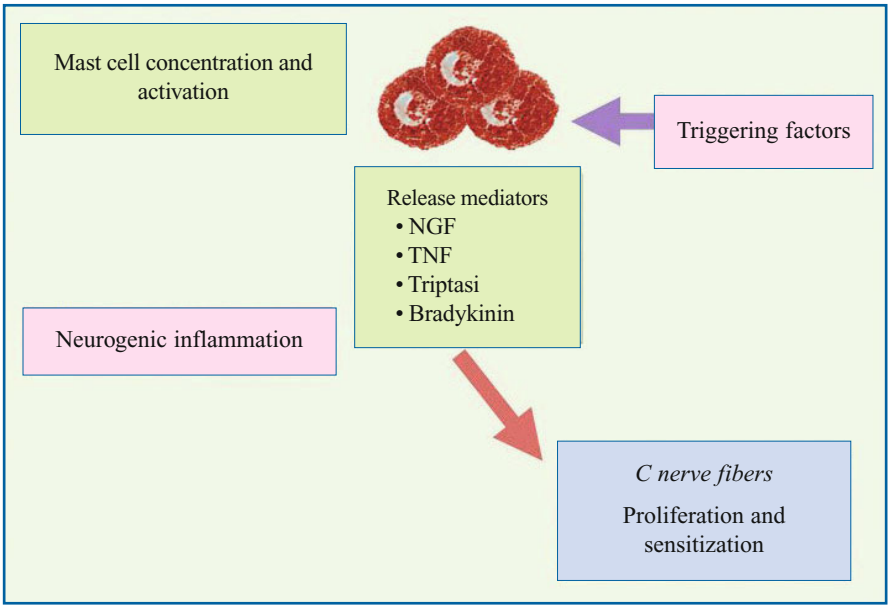

Fig. 6.4 Neurogenic inflammation

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It is clear that recurrent Candida albicans infection may play a central role in the triggering of vestibulodynia.

Conversely, others have found no evidence for active tissue inflammation in vestibulodynia patients, as assessed by inflammatory markers (cyclo-oxygenase-2 and inducible nitric oxide synthase) that are usually up-regulated during the inflammatory process.

In vulvodynia patients there is no *active inflammation*, rather we find a *neurogenic inflammation*, particularly in vestibulodynia patients, where prolonged or severe infectious, thermal or chemical irritation causes excessive local responses (mast cell activation).

It is our opinion that the inflammatory character of vestibulitis can be reconsidered, thus justifying its nosological name (see Chapter 2).

The morphological findings of nerve-ending proliferation has not been demonstrated for generalized vulvodynia, but new elements have been identified in this subtype of disease where there is a scarcity of research on the pathophysiology.

As with patients with neuropathic pain, women with generalized vulvodynia exhibit hyperalgesia and/or allodynia, which can be considered a functional effect corresponding to neural hyperplasia. Our recent study indicates that the current perception threshold (CPT) values were lower in women affected by vulvodynia than those in controls, suggesting a hypersensitivity (Fig. 6.5).

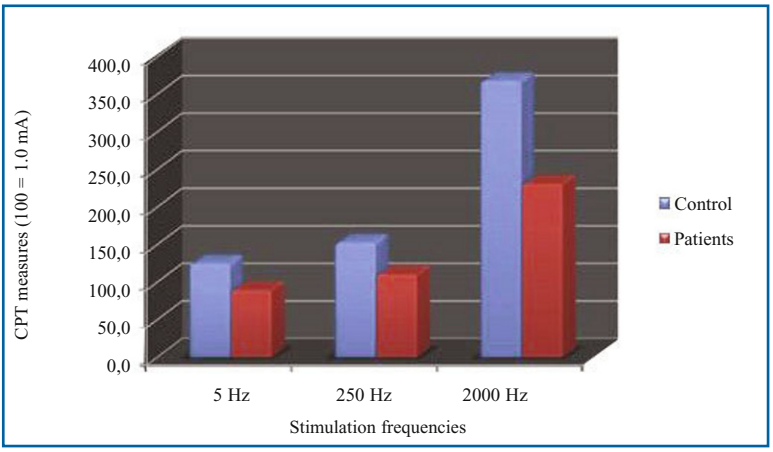

Fig. 6.5 Results of current perception threshold (CPT) measures in 3 selected stimulation frequencies (2,000-, 250-, and 5-Hz) in healthy volunteers (control) and in women with a diagnosis of generalized vulvodynia (patients). Each stimulation frequency reflects the pattern of sensory function of the 3 major sensory fiber types (Aβ, Aδ, and C). Women with vulvodynia showed mean CPT values significantly lower than the controls did at each frequency ($p < .01$) (Murina F et al., 2010)

The CPT measures provide objective and quantitative determinations of the sensory nerve conduction and nerve functional integrity, and it uses an electrical stimulus selective for the large and small myelinated and unmyelinated fibers that are involved in the transmission of painless and painful sensation.

Each of the three major sensory fiber types has a characteristic neurophysiological profile, sensory function, sensation evoked by electrical stimulation, and conduction block susceptibility. Because findings of enhanced pain perception are typical of neuropathic pain syndromes, our results add strength to a neuropathic hypothesis for pain also in generalized vulvodynia (see Fig. 6.5).

Triggers

It is always difficult to find a trigger for inflammatory events in generalized vulvodynia. Women with generalized vulvodynia experience symptoms anywhere within the distribution of the pudendal nerve (Fig. 6.6).

The pudendal nerve is an extrapelvic nerve; it quickly exits the pelvis, wraps around the ischial rectal fossa, enters the pudendal canal, and provides innervations to the external genitalia, the urethral sphincter, the anal sphincter, and the vagina. The branch that innervates the vulva and vestibule is very superficial, while the branch that innervates the clitoris is deeper. Thus, there is the possibility of repeated micro-trauma to the vulvar branch, for example during bicycling and horseback riding, which could lead to neurogenic inflammation.

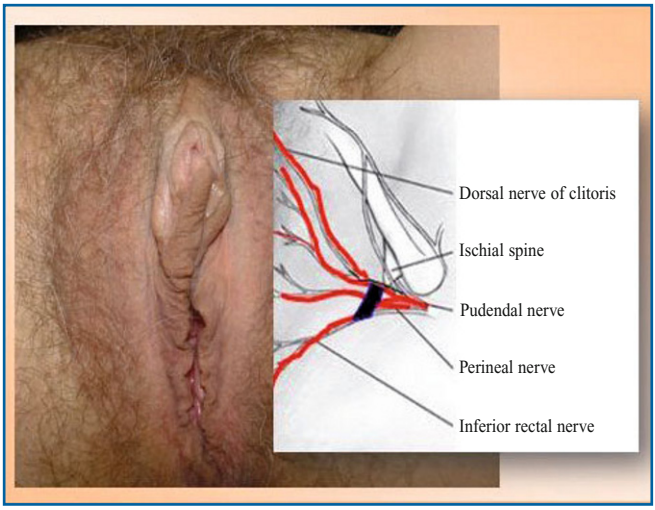

Fig. 6.6 Vulvar pudendal nerve distribution

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Several lines of investigation support the elements of central sensitization in vulvodynia patients.

Particularly, some authors have demonstrated that vestibulodynia patients perceive light and moderate touch to the vulvar vestibule more intensely than do control women. The increase in perception is reflected in more significantly activated neural areas than in control women. In addition, it has been shown that vestibulodynia in young women is associated with increased gray matter density in pain modulatory and stress-related brain regions. It has been speculated that increased gray matter density could be caused by microglial proliferation, maybe due to excess excitatory neural activity.

Box 2. Central Sensitization

- Increased pressure sensitivity in both the vulva and peripheral body regions
- Increased pain intensity and unpleasantness in response to tender-point examination in non-genital sites
- Higher levels of brain activity in primary and secondary somatosensory cortices during application of pressure to the posterior vestibule
- Lower pain pressure thresholds to noxious cold stimulation, suggesting a systemic hypersensitivity
- Higher gray matter density in pain modulatory and stress-related areas

Modified from Vulvodynia: Integrating Current Knowledge into Clinical Practice, by the National Vulvodynia Association, 2010 (www.nva.org), with permission

This description of vulvodynia is supported by a good deal of evidence, but there are some open questions regarding its etiology, including:

What Is the Relationship Between Vestibulodynia and Generalized Vulvodynia?

Some clinicians think that provoked vestibulodynia and generalized vulvodynia may be variations in severity of the same disorder. The etiopathological process has been suggested to first result in the localized pain of vestibulodynia and then progress to the chronic, generalized vulvar pain; instead, our experience suggests that the two conditions may be two distinct disorders. The two subtypes of vulvodynia can be clearly distinguished by some characteristics such as age, symptoms and triggering

inflammatory factors. Nevertheless, individuals may have aspects of both vestibulodynia and generalized vulvodynia, with overlapping symptoms.

There are many problems with this hypothesis, such as patients who have prolonged vestibulodynia without ever developing generalized vulvodynia, and those, whose condition starts with generalized vulvar pain but never develop introital dyspareunia. The common element is that both of these conditions represent a form of vulvar reflex-sympathetic neuropathic pain with sensitization of nociceptive C fibers, so that touch sensation is replaced with an experience of pain.

In our opinion a different subtype of vestibulodynia exists that is distinguishable by certain characteristics such as trigger factors, age, pelvic floor dysfunction and comorbidities, rather than two diseases classified upon the vulvar symptoms localization and characteristics of pain (provoked or unprovoked).

What Is the Role of Pelvic Floor Dysfunction?

Electromyographic studies of the pelvic floor in women with unprovoked pain have shown differences compared with asymptomatic patients. Pelvic floor hypertonic dysfunction is found in 80% to 90% of patients with vulvodynia. A relevant topic to be investigated is whether vulvodynia reflects pelvic floor dysfunction with trigger points of pain, or whether it is a form of referred pain, or a result of dysfunctional nerve fibers in the pelvis.

In vulvodynia, there is obviously nerve involvement in pain. The leading opinion indicates that vulvar pain can produce spasm of the levator ani muscle, and pelvic floor hypertonicity contributes to self-maintenance of pain. In summary, the levator ani muscles are innervated by the levator ani nerve, while no evidence of innervation by the pudendal nerve can be found. The levator ani motor neurons are diffusely distributed in the sacral ventral horn, while the pudendal motor neurons are concentrated in Onuf's nucleus (a group of neurons located in the ventral part of laminae IX of the anterior horn; see Fig. 6.3). However, there is a great deal of overlap between the dendrites of levator ani motor neurons and pudendal motor neurons, and both nerves contain primary afferent fibers that project into the sacral spinal cord. Thus, there is great potential for interaction between the sensory and motor nerve fibers that control the levator ani muscle, the vulva, and the vestibule. It is not important what starts the process (muscle or nerve) but it is important how alteration of the pelvic muscles is responsible for the severity of symptoms.

Indeed, *"the weight of the muscle"* may be different between patients with vulvodynia and this is the only important target of the treatment program.

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What Is the Role of Hormonal Alteration as a Potential Cause of Vulvodynia?

Some studies have concentrated on the effects of estrogen on peripheral nervous system pathways, emphasizing those that pertain to pain. A review of the literature reveals a somewhat common idea that there is a relationship between estrogen and sensation, and that a decrease in threshold occurs with increased estrogen levels, such as during the menstrual cycle, pregnancy, and estrogen replacement. This may explain a change in symptoms during the menstrual cycle; in fact some vulvodynia patients can have an exacerbation of symptoms during the premenstrual period. Furthermore, the vulvar vestibule is embryologically analogous to the urogenital gland in males. These glands have a high density of androgen receptors, which implies that adequate testosterone levels are essential for the maintenance of healthy vestibular tissue.

It is unclear whether oral contraceptives (OC) play a role in the development of vulvodynia. Some clinicians propose that the use of OCs, particularly at an early age, down-regulates estrogen receptors in the vulvovaginal tissue, causing an altered morphological pattern in the vulvar vestibule; the epithelium can appear thin and fragile and a decrease of lubrication can be observed. OC use has been associated with a 7-fold increase in the risk of developing vestibulodynia. The risk is higher with current, long-term or early use, and with use of OCs of high progestogenic potency and low estrogenic and androgenic potency. Until a causal effect is demonstrated, however, women should not be discouraged from using OCs, but should be made aware of vestibulodynia.

In a notable study published in 2004, Bernard Harlow showed that women taking oral contraception who reported vestibulodynia were much more likely to have difficulty or be unable to use tampons for menstrual protection. This would suggest the presence of hyperactivity of the levator ani prior to first coitus (lifelong or primary) which may be associated with moderate vaginismus. Muscular contraction mechanically restricts the vaginal opening, predisposing the woman to pain upon initial penetration, reflex inhibition of lubrication with consequent vaginal dryness, and microabrasions of the mucosa of the vaginal opening, thus favouring chronic inflammation, the proliferation of pain nerve fibers and a further increase in the defensive contraction of the levator ani.

TIP: The examination of a patient taking oral contraception who reports "vaginal dryness and/or painful coitus" should therefore consider:

1. whether the levator ani is hypertonic. If so, teach the patient to relax the muscle with various techniques, including stretching, physiotherapy and electromyographic biofeedback;
2. the vaginal pH. If higher than 5, this is a sign of little oestrogen impregnation and an indication to increase the oestrogen level of the pill, commence local oestrogen therapy or at least to use vaginal acidifiers to improve the composition of the vaginal ecosystem.

Otherwise there is the risk of blaming the contraceptive pill, which merely acts as a litmus test indicating other problems relating to muscles, the vaginal ecosystem and/or fear of coitus which deserve to be treated in an appropriate manner.

How Relevant Are Psychosexual Factors in Vulvodynia Patients?

Psychological morbidity is significantly higher in women with vulvodynia compared with asymptomatic women. Many studies demonstrate high degrees of anxiety, depressive symptoms, somatization disorders and hypochondriacal symptoms in vulvodynia patients.

While some propose that the syndrome has a purely psychogenic origin, the leading opinion suggests that sexual dysfunction and psychological distress are the consequence rather than the cause of vulvodynia. However, this concept is still under debate.

The anterior cingulate brain cortex (ACC) contributes to the control of the state of conscious arousal and attention based on prefrontal cortical innervations. Anxiety dependent pain exacerbation is also mediated by other limbic structures, such as the hippocampus. A history of abuse or trauma is common in chronic pelvic pain patients, and this is also mediated by limbic dysfunction, particularly of the ACC, hippocampus, and amygdala.

It has been observed that vulvodynia patients have higher rates of sexual abuse, including threatened sex, forced intercourse, lifetime sexual victimization and severe child sexual abuse, an association that appears to hold true for other vulvodynia comorbidities such as irritable bowel syndrome (IBS) and interstitial cystitis (IC). Although there is a degree of association, several studies have refuted the notion that prior sexual and/or physical abuse is a predisposing factor for vulvodynia.

Regardless of the sequence of events, physical and psychological factors produce a continuum with multiple dimensions of pain. Studies show

lower frequency of intercourse, decrease in desire and increased difficulty achieving orgasm, and many patients with vulvodynia who do have intercourse do so out of a sense of obligation rather than desire.

In conclusion, it is still impossible to say whether psychosexual factors are involved in the development or maintenance of vestibulodynia, or whether they are the consequence of an undiagnosed, persistent and debilitating pain. Pain modulation by psychological factors is one of the most complex problems; in vulvodynia patients, psycho-neurobiological vulnerability plays a relevant role and the experience of pain varies depending on the patient's psychological state.

Why Is There a Frequent Association Between Vulvodynia and Other Chronic Pain Conditions?

Vulvodynia is frequently associated with bladder pain syndrome (BPS/IC), IC, a urological condition of urinary urge, frequency and bladder spasms, IBS, and fibromyalgia, a condition encompassing pervasive muscle pain and sleep disorder. All these conditions share a common denominator: a chronic inflammation, which is the major contributor of chronic pain and related symptoms. Histological data (from the colonic mucosa in IBS, from the bladder wall in BPS, from the vulvar vestibule in vulvovestibulitis, and from deep endometriosis in the pelvis and/or abdomen), show three common findings in the examined specimens: significant increase of mast cells; significant increase of degranulated mast cell, suggestive of a very active inflammatory state; significant increase of mast cells close to pain nerve fibers. These findings support the close relationship between chronic inflammation and chronic pain and suggest that the hyperproduction of inflammatory molecules (interleuchines 1 and 8, tumor necrosis factor alpha etc.) may contribute to local and systemic comorbidities. New data suggest that depression may be caused/worsened by the flooding of the brain, by the inflammatory molecule produced by the hyperactive mast cells typical of chronic inflammation. The frequent overlap of irritable bowel syndrome, interstitial cystitis, vulvodynia, and other chronic pelvic pain disorders may be indicative of aberrant neuronal interactions or reflexes, such that the irritation of one organ leads to co-sensitization of others. With continued irritation, neurotrophic factors produced by both smooth muscles and sensory neurons may influence neurite outgrowth and axonal sprouting, which could lead to motor and sensory changes in target organs.

How to Make a Comprehensive Diagnosis of Vulvodynia and its Comorbidities

7

Vulvodynia is a diagnosis of exclusion, a pain syndrome with no other identified cause.

Medical History

A patient's medical history provides essential information in the determination of a correct diagnosis of vulvodynia. It is important to ask specific questions in order to obtain detailed information, and equally essential to ask open-ended questions that allow a patient to describe her condition, throughout the whole process, displaying empathy, understanding, and acceptance (see Chapter 3).

Box 1. The targeted history of vulvodynia patients

- Current symptoms
- Personal habits (hygiene, typical diet, etc.)
- Past medical and surgical history
- Obstetric and gynecologic history (menstrual function, contraception, previous vulvar infections, etc.)
- Medications and allergies
- Sexual history and psychological profile
- Bladder and bowel function

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Personal habits is a fundamental aspect to consider; eliminating all possible irritants is an important step. If patients are using topical creams with an irritating base - as is often the case - they have to inform the clinician. The daily use of a potentially irritating mini-pad or panty-liner is not healthy for any woman and many lubricants also contain irritants as preservatives.

It is also important to recognize certain aspects of a patient's medical history such as bladder and bowel function. It has been estimated that more than half of vulvodynia patients have symptoms of excessive urgency and frequency of urination and suprapubic pain. This condition is defined painful bladder syndrome/interstitial cystitis (PBS/IC). PBS/IC is a chronic, severely debilitating disease of the urinary bladder with a course that is usually marked by flare-ups and remissions. Dyspareunia is not uncommon in persons with PBS/IC and may be related to the mechanical effects of intercourse on the inflamed bladder.

Box 2. Diagnostic criteria for painful bladder syndrome /interstitial cystitis (PBS/IC)

- Presence of urinary urgency or frequency, or pelvic/perineal or bladder pain
- Presence of glomerulations (pinpoint submucosal hemorrhages) or ulcers on cystoscopic examination with hydrodistension under anesthesia (interstitial cystitis)
- Absence of genitourinary infections
- Absence of neoplastic diseases or benign bladder tumor
- Absence of history of radiation, tuberculosis or chemical cystitis

Irritable bowel syndrome (IBS) is a very common functional gastrointestinal disorder characterized by abdominal discomfort, bloating, and disturbed defecation. Many IBS patients have at least one comorbid somatic complaint and many meet diagnostic criteria for other functional disorders

Several studies have reported an increased prevalence of sexual dysfunction among IBS patients, including increased dyspareunia and more severe IBS symptoms following intercourse. The studies are consistent in their finding that the overlap among these disorders (vulvodynia - PBS/IC - IBS) is greater than expected based on their separate prevalence rates. In addition, patients with more than one disorder have greater disease severity, higher rates of psychopathology, and more severely impaired health-related quality of life than those with only one disorder.

It is also essential to develop a history of medication use and compare it to the timeline of the patient's vulvodynia history. Many vulvodynia patients use prescription medications for anxiety and depression, often secondary to vul-

var pain. Sexual dysfunction may affect the majority of patients taking some psychotropic drugs, as a predictable outcome of the same neurotransmitter effects that underlie the agents' therapeutic action. Such predictable forms of sexual dysfunction include the orgasmic disturbances and the diminishment of sexual desire associated with serotonin-reuptake inhibitor antidepressants (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine. Benzodiazepines, particularly in the higher doses often used for panic disorder, have been most strongly associated with decreased libido.

Antibiotics are a frequent prescription medication that vulvodynia patients use as a consequence of a vaginal swab; in fact we can find commensal bacteria such as streptococci, diphtheroids and coagulase-negative staphylococci without any responsibility on vulvar pain. Antibiotics do not directly cause vulvodynia but their repetitive and improper use are thought to predispose women to vulvovaginal candidosis by eliminating the protective bacterial flora, thus allowing *Candida* overgrowth in the gastrointestinal tract, vagina, or both. In particular, *Lactobacillus* spp. could provide colonization resistance and prevent germination, maintaining low numbers of yeast.

The psychosocial evaluation should include information about the presence of psychologic symptoms (e.g., anxiety, depression, anger), psychiatric disorders, personality traits or states, and coping mechanisms. Evidence of stress levels, degree of support from others, including partner or family, should also be noted. It is important to ask women about all aspects of their sexual function and satisfaction (see Chapter 3).

Physical Examination

The first important aspect of physical examination is the visual inspection of vulvar region (Fig. 7.1). It requires a meticulous and methodical examination of the vulva, including the perineum and perianal region.

Box 3. The targeted physical examination of vulvodynia patients

- Vulvar region:
  - visual inspection and vulvoscopy
  - palpation
  - Q-tip test
- Pelvic floor evaluation
- Vaginal inspection
- Bi-manual palpation

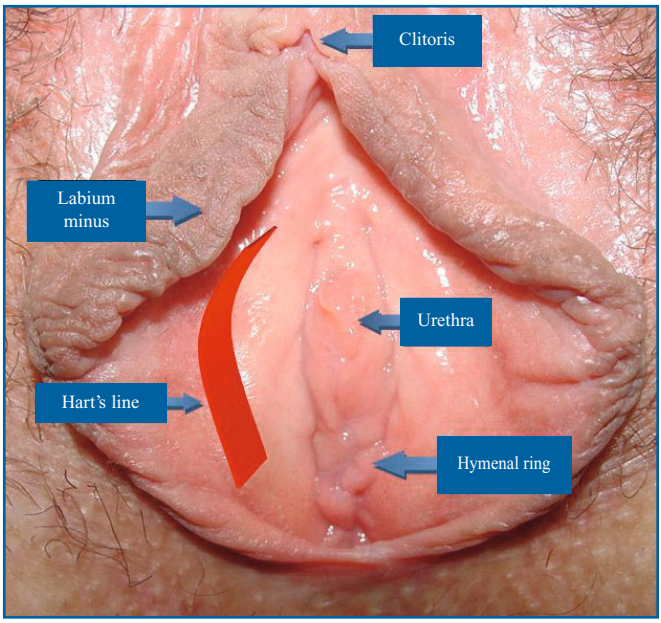

Fig. 7.1 Vulvar anatomy

Vulvoscopy, the colposcopic examination of the vulva, gives the examiner the ability to characterize any lesions with much greater detail. For example, the vulvoscopist can determine if a lesion is a raised plaque or just a flat macule. In addition, the margins of the lesion can be characterized (e.g., are the lesions distinct or are the observed changes more diffuse?).

Vulvoscopy enhances the ability to detect:

- *Color changes* associated with inflammatory or neoplastic diseases of the vulva:
  - red areas can be visualized when there are stromal changes due to inflammation, vulvar dermatoses, or neovascularization in association with neoplasia;
  - white areas can be found when there is a decreased vascularization, fibrotic changes in the stroma and increased keratinization (lichenification).
- *Scarring and architectural changes*: Chronic inflammatory disorders of the vulva, such as lichen sclerosus and lichen planus, frequently cause structural changes such as resorption of the labia minora, vulvar granuloma fissuratorum (chronic tearing of the posterior fourchette), and phimosis of the clitoris.
- *Subtle lesions such as tiny fissures,* which may be very painful.

Therefore, the vulvoscopist's main goal in suspected vulvodynia is to rule out specific diseases that can cause vulvar pain.

Box 4. Evaluating abnormalities of the vulvar skin

- Color
- Texture
- Integrity: flattening of the labia minora, asymmetry, agglutination, synechial formation anteriorly and/or posteriorly

Diagnoses to Rule out

Skin diseases of the vulva or vagina can also cause pain. Lichen sclerosus, lichen planus, and lichen simplex chronicus are three of the most common non-neoplastic epithelial disorders of the vulva.

Lichen sclerosus (LS) is a non-neoplastic chronic lymphocyte-mediated inflammatory dermatosis with distinctive dermal sclerosis and a predilection for the anogenital skin in women. Itch is the main symptom but pain occurs if there are erosions or fissures. Dyspareunia occurs in the presence of erosions, fissures or introital stenosis. There is typically no genital mucosal involvement, but the stenosis that may develop at the edge of mucocutaneous junctions can cause severe dyspareunia.

The clinical features of lesions are variable depending on the stage and severity of the disease. Patchy involvement is seen in some, while others have extensive, confluent disease (Fig. 7.2). Areas of pale, thinned, wrinkled, atrophic skin, possible telangiectasia and haemorrhagic blisters, may be evident at sites of lesions (Fig. 7.3). Lichenification or hyperkeratosis may also be the prevalent pattern.

Progressive sclerosis can lead to loss of normal genital structures. Labia minora may become fused or resorbed, the clitoris may be buried and the introitus significantly narrowed.

LS in females has two peak ages of presentation. The first of these occurs in *prepubertal girls* (7.4) and may resolve or continue beyond the menarche. The other peak of incidence is in *postmenopausal women*.

It is important not to confuse childhood sexual or physical abuse with prepubertal lichen sclerosus (Figs. 7.4 and 7.5).

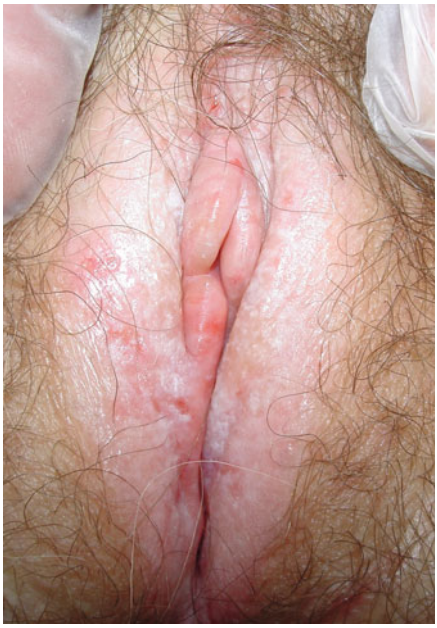

Fig. 7.2 Lichen sclerosus

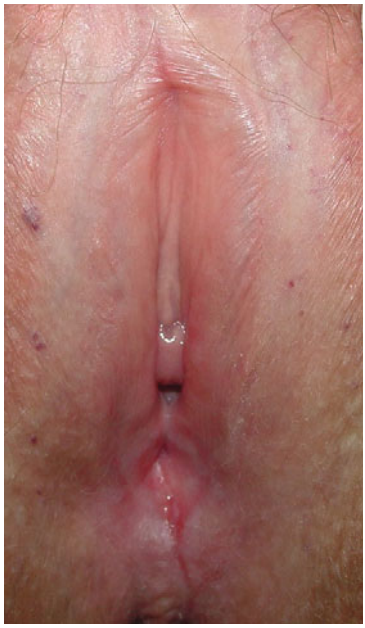

Fig. 7.3 Lichen sclerosus

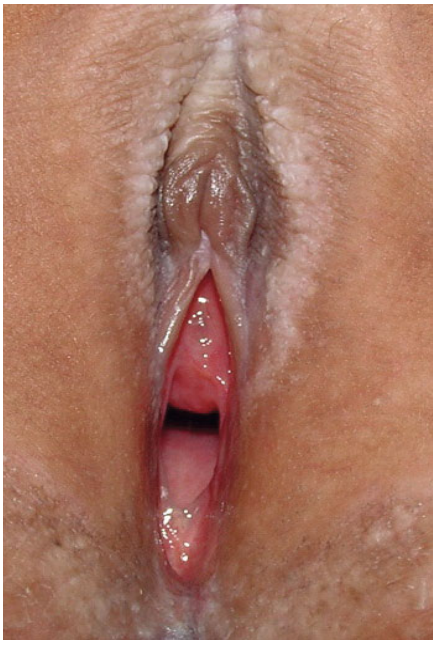

Fig. 7.4 Prepubertal lichen sclerosus

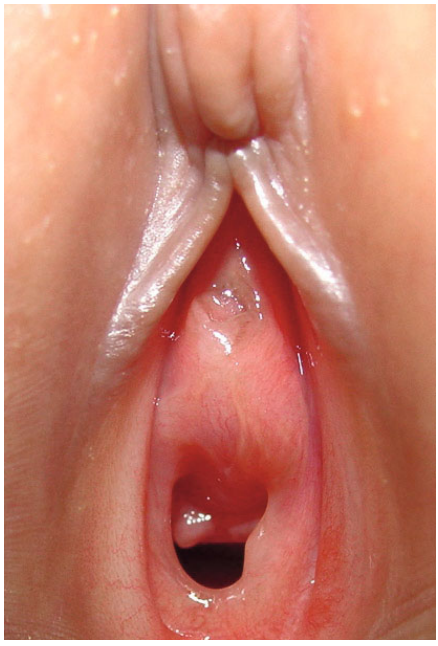

Fig. 7.5 Childhood sexual abuse

Lichen planus (LP) is an inflammatory autoimmune disorder involving keratinized and mucosal surfaces. There are three clinical variants that affect the vulva: erosive lichen planus, papulosquamous lichen planus, and hypertrophic lichen planus.

Vulvovaginal involvement can be associated with itching, burning, pain, dyspareunia, and destruction of the vulvar and vaginal architecture. The variant that typically affects the vulva and vagina is called erosive LP and this is the most painful form of the disease (Fig. 7.6).

The main symptoms are vulvar burning, occurring spontaneously or after vulvar contact, and severe dyspareunia. In LP the mucosa of the introitus is often denuded with a red, glazed appearance; there may be erythema of the vestibular mucosa with varying degrees of epithelial desquamation or frank erosions.

Lichen simplex chronicus is not a specific entity, but rather describes lichenification of the vulva caused by persistent itching and scratching. The skin can become leathery and thickened or, in severe cases, may be excoriated (Fig. 7.7). Vulvar pain, if present, is usually a result of irritation from open lesions.

Many different diseases may produce erosive, ulcerative, or desquamative lesions of the vulva; ***vulvar aphthae*** and ***genital herpes*** are the two

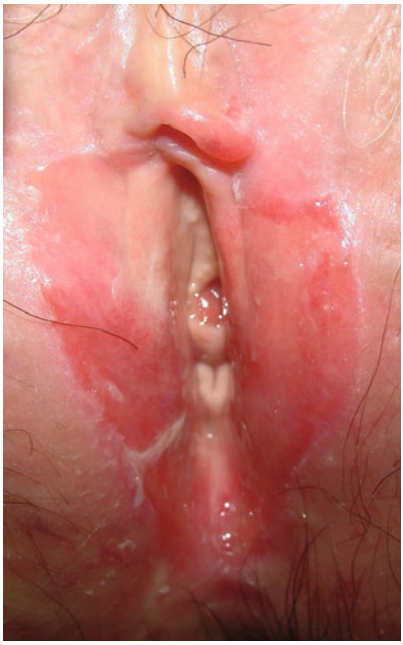

Fig. 7.6 Erosive lichen planus

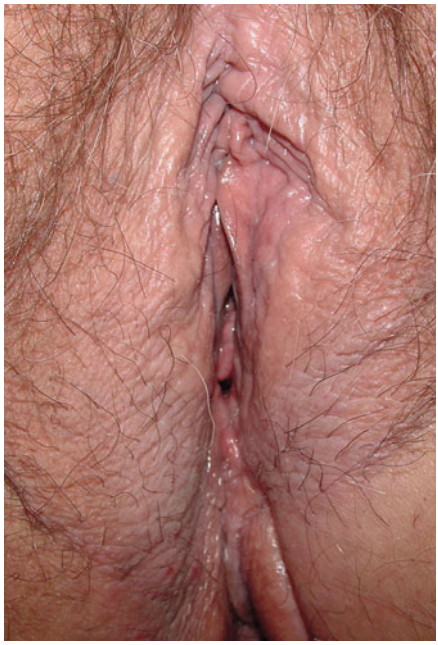

Fig. 7.7 Vulvar lichen simplex

common ones. *Vulvar aphthae* are small, shallow ulcers with a yellow base and erythematous rim. They occur acutely and resolve over a few day, and are quite painful. Although attacks tend to be intermittent, they can be very frequent or almost continuous in some patients. Women with vulvar aphthosis frequently have oral aphthae (Fig. 7.8).

Vulvar aphthae are commonly confused with genital herpes, and this is hardly surprising, given that they are painful, acute, recurrent ulcers. The difference is that genital herpes, once past the very brief blister stage, has the appearance of an erosion rather than the typical deeper, ulcerative lesions that are seen in the mouth (Fig. 7.9).

The mucosa of the labia minora and vestibule is generally pink and smooth; however, localized or widespread micropapillary or villiform patterns may sometimes be observed (Fig. 7.10). These can be misinterpreted as **condyloma due to human papillomavirus (HPV)** infection.

Vulvar micropapillomatosis should be left untreated; laser removal, for example, frequently results in an 'iatrogenic' trigger for vestibulodynia development (Table 7.1).

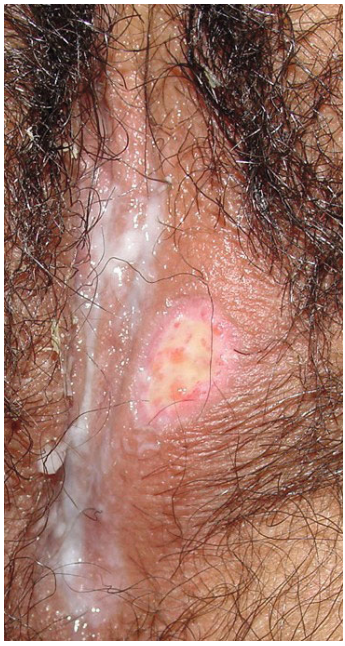

Fig. 7.8 Vulvar aphthous ulcer

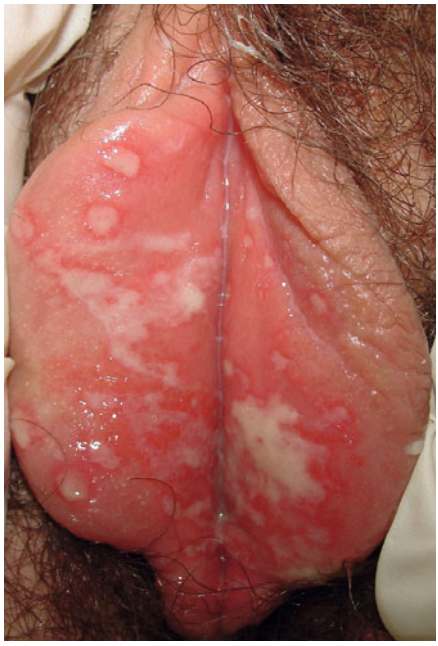

Fig. 7.9 Vulvar herpes simplex

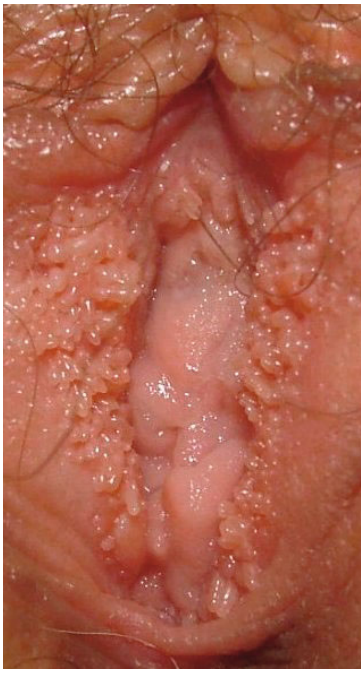

Fig. 7.10 Vulvar micropapillomatosis

Table 7.1 Differentiating vulvar micro-papillomatosis from vulvar condilomas

Vulvar micropapillomatosis	Vulvar condilomas
• Regular shape and distribution	• Small bumps
• Uniform color	• Flat or verrucous
• Soft consistency	• Reddish or brown, smooth
• Lack of tendency to fuse	• Dome-shaped lesion on keratinized skin

Vulvar intraepithelial neoplasia (VIN) does not have a characteristic presentation. Some patients may have pruritus or burning, while others will notice an asymptomatic abnormality on the vulvar skin. The lesions may be raised or flat with a rough surface. The lesions may appear white or red or of mixed color (Fig. 7.11).

Vestibular tenderness is assessed by applying a cotton tipped swab (the Q-tip test; Fig. 7.12) to the vulvar vestibule in a clock-like pattern. Gentle touch provokes either hyperesthesia, a heightened intensity relative the degree of applied pressure, or allodynia, the perception of a different sensation to that applied (e.g., pain rather touch).

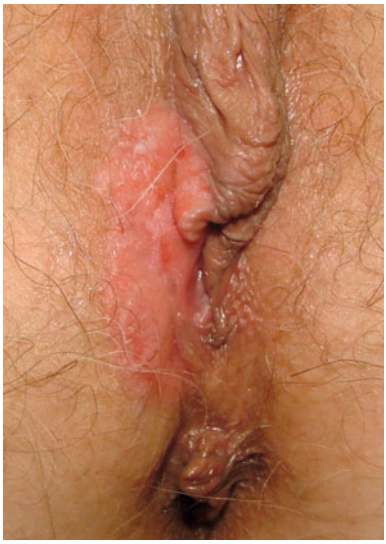

Fig. 7.11 Vulvar intraepithelial neoplasia

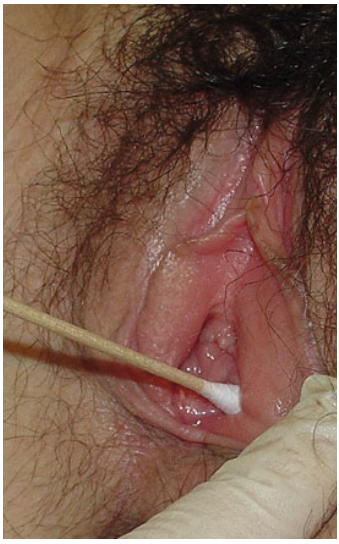

Fig. 7.12 Cotton swab test

Thresholds to pain provoked by pressure are markedly lower in provoked vestibulodynia patients. Pain is typically most severe in the posterior vestibule between the 5 and 7 o'clock positions, but can occur anywhere within the vestibule.

The Q-tip touch test has been validated as useful in identifying the exact location of the pain and enabling the patient to classify the areas where it is *mild, moderate, or severe*. A diagram of pain locations is helpful in assisting the assessment of pain over time.

Provoked vestibulodynia patients have reported significantly higher pain ratings at the vulvar vestibule than pain-free controls, demonstrating the utility of this test in distinguishing between vulvodynia patients and control women.

Pelvic Floor Evaluation

Box 5. Pelvic floor markers to investigate in vulvodynia patients

- Tenderness
- Trigger points
- Hypertonus
- Decreased mobility

Clinical evaluation of the pelvic floor begins with simple observation of pelvic floor muscle activity during the process of squeezing and relaxation. The simple observation of the perineum and introital area in the dorsal lithotomy position during the performance of a Kegel squeeze is often quite revealing. The woman squeezes the muscles used to stop the flow of urine for about 10 seconds, and then relaxes them for about 10 seconds.

Patients with pelvic floor hypertonic dysfunction often have so much muscle tension at 'rest' that they are unable to produce more contractile strength and therefore cannot produce an effective squeeze. It can be revealed by a 'short perineum', conventionally with a length above 2 centimeters.

At this point the examiner, if accepted by the patient, should place a generously lubricated single finger in the vagina to assess pelvic floor awareness and the ability to squeeze and relax the levator ani. Many scales are available to document strength, tone, and tenderness, yet all these scales are subjective and unvalidated. We usually used a simple empiric score that allows us to reproduce pelvic floor hypertonus with an acceptable reliability.

Box 6. Pelvic floor hypertonicity score

0	No hypertonicity
1	Mild hypertonicity
2	Moderate hypertonicity
3	Severe hypertonicity

Many patients will be found to be most tender along the lateral border of the levator ani, which is where the levator muscles insert onto the arcus tendineus levator ani.

Muscular pain can be assessed with insertion of one finger at the introitus as the patient performs a series of contraction and relaxation exercises. Spontaneous or elicited pain in the lower third of the anterior vaginal wall should be carefully explored, as it may be associated with bladder-related comorbidities (cystalgia, urethralgia, post-coital cystitis, intersitial cystitis) that are reported in one third of vulvodynia patients.

Vaginal Inspection

The vagina should be examined for possible evidence of atrophy, ulcerations or abnormal discharge. Secretions should be collected from the later-

al vaginal walls using a swab. It is recommended that in the assessment of women with vaginal discharge (Table 7.2), vaginal pH is checked, using narrow range paper (pH 4–7). pH is normal (4.0–4.5) in vulvovaginal candidosis, and pH in excess of 4.7 usually indicates bacterial vaginosis, trichomoniasis, or a mixed infection. A wet mount or saline preparation should be done routinely to identify the presence of yeast cells and mycelia but also to exclude the presence of so-called clue cells indicative of bacterial vaginosis and motile trichomonads. A 10% potassium hydroxide preparation is more sensitive than a saline preparation in identifying yeast or hyphae (65–85% sensitivity).

Table 7.2 Causes of vaginal discharge in women of reproductive age

Physiological
Infective (non-sexually transmitted)
- bacterial vaginosis
- *Candida*
Infective (sexually transmitted)
- *Trichomonas vaginalis*
- *Chlamydia tachomatis*
- *Neisseria gonorrhoeae*
Non-infective
- foreign bodies (tampons, condom)
- cervical polyps or ectopy
- genital tract malignancies

Tests

Histopathology, traditionally, has been of little value except to exclude other conditions. Biopsies are not generally performed when the physical examination and history have ruled everything else out. The routine use of magnetic resonance imaging (MRI) is usually recommended in patients with unprovoked pain. MRI may not be necessary, however, as the incidence of pathology, for example sacral cysts, causing referred pain to the vulva is very low. Pelvic floor surface electromyography (EMG) is a test that should not be performed routinely.

Objective identification of pelvic floor hypertonic dysfunction can be obtained using various techniques. The most common is surface EMG, which is often performed as a part of a pelvic floor evaluation by physical

therapists and nurse clinicians trained in the evaluation and management of patients with pelvic floor dysfunction. In patients with hypertonic dysfunction we find the following (listed in order of prevalence):

- elevated and unstable resting baseline activity;
- poor recovery, poor postcontraction and relaxation;
- spasms with sustained contractions and poor strength.

How to Treat Vulvodynia

8

Treatment for any medical disorder should be directed at the underlying mechanisms or pathophysiological processes involved.

This is difficult to achieve with vulvodynia in view of the heterogeneity of factors involved in the etiology of the disorder. Indeed, vulvodynia may be a final result of or common pathway for several pathological processes, such that any one management strategy may not be adequate for all women complaining of vulvar pain.

Many women with vulvodynia experience loss of hope, which can lead to psychological, and emotional issues. Treatment should be holistic and focus not only on the primary site of pain but on its subsequent impact on the patient's lifestyle and sexual functioning.

A lead clinician should triage patients and consider referral to other healthcare professionals who are experienced in the management of vulvodynia, e.g. Urologist, Physiotherapist, Gastroenterologist, Clinical Psychologist, and pain-management teams.

It is recommended that the patient be asked about the types and outcomes of treatment she may have already used. It is important to bear these in mind, but the clinician should remember that not all treatments are delivered in the same fashion by all providers, and that not all patients adhere to treatment regimens as recommended.

Multimodal and multidisciplinary interventions should be part of a treatment strategy for patients with vulvodynia. *Multimodal* interventions constitute the use of more than one type of therapy for the care of patients with chronic pain. *Multidisciplinary* interventions are multimodality

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approaches in the context of a treatment program that includes more than one discipline. The literature indicates that the use of multidisciplinary treatment programs compared with conventional treatment programs is effective in reducing the intensity of pain reported by patients.

Box 1. The aims of therapy for vulvodynia

- Optimize pain control, recognizing that a pain-free state may not be achievable
- Enhance functional abilities, and physical and psychologic well-being
- Enhance the quality-of-life of patients
- Minimize adverse outcomes

Treatment guidelines recommend a standard treatment algorithm for all women with vulvodynia, but we believe that a more *personalized guided* approach is needed, constructed using 'end points' that reflect differences within patients with vestibulodynia or generalized vulvodynia. The proposal is derived from a cluster analysis of patients that explored whether subgroups exist among women with vulvodynia with respect to pain-related and personality variables.

Box 2. End-points for vulvodynia therapy

- Reduction of triggers and irritating stimuli
- Peripheral nociceptive blockade
- Central inhibition
- Limit associated pelvic floor dysfunction
- Limit psychosexual dysfunctions of the syndrome

Reduction of Triggers and Irritating Stimuli

We recommend that the patient initially be encouraged to follow general advice for minimizing vulvar irritation. This is the first level of treatment that each physician must recommend to any patient with vulvodynia.

Box 3. Vulvar care measures to minimize vulvar irritation

- Avoid vulvar irritants (perfumes, dyes, shampoos, detergents) and douching
- Using adequate lubrication for intercourse
- Wear all-white cotton underwear
- Wear loose-fitting pants or skirts; do not wear pantyhose
- Use dermatologically/gynecologically approved intimate detergents
- Use soft, white, unscented toilet paper
- Avoid getting shampoo on the vulvar area
- Do not use bubble bath, feminine hygiene products, or perfumed creams or soaps
- Urinate before the bladder is full
- Prevent constipation by adding fiber to your diet and drinking at least 8 glasses of water daily
- Use 100% cotton menstrual pads and tampons
- Use a water-soluble lubricant during sexual activity
- Apply ice, or a frozen blue gel pack (lunchbox size), wrapped in a single layer of towel to relieve burning after intercourse
- Urinate (to prevent infection) and rinse vulva with cool water after sexual intercourse
- Avoid exercises that puts direct pressure on the vulva such as bicycle riding and horseback riding
- Limit intense exercise that create a lot of friction in the vulvar area (try lower intensity exercises such as walking)

Adapted from 'Self-Help Tips for Vulvar Skin Care', National Vulvodynia Association (http://www.nva.org/Self_Help_Tips.html)

Topical agents in general should be avoided in order to avoid the problem of irritation and exacerbation of symptoms. Skin reactions to topical medications are not uncommon, and it is often the base that the cream or gel is to blame rather the active ingredient.

Topical lidocaine gels or ointments can be used in women with provoked vestibulodynia making penetrative sex possible. It is generally advised that the gel or ointment is applied 15–20 minutes prior to sex, and patients should to be warned of the possibility of irritation.

In a study in a group of patients with vulvodynia (mainly provoked pain), 5% lidocaine ointment was applied liberally to the affected area at night, and then a cotton wool ball soaked in 5% lidocaine was inserted

into the vestibule and left overnight. At follow-up there was an improvement from 36% to 76% of women reporting the ability to have intercourse.

Some reactions are associated with topical anesthetics such as stinging, erythema and edema. Benzocaine, an anesthetic frequently found in over-the-counter topical preparation, should be avoided due to its frequent association with allergic contact dermatitis. It is also important to warn patients of the potential affects on the partner, such as penile numbness (male partners may prefer to wear condoms). Partners should also be advised to avoid oral contact.

Lidocaine can burn when applied, but can be mixed with a little vaseline (the use of vaseline can reduce the lidocaine burning effect). If the patient cannot tolerate this, consider 2.5% lubricant jelly.

Topical compound of estradiol applied to the vestibule can be helpful in women with a pale and thin vestibular surface. *Recurrent yeast* should be considered as a triggering factor (see Chapter 6). In this case, long term maintenance therapy with a suppressive prophylactic regimen may be required. Weekly treatment with fluconazole (150 or 200 mg) for 1-2 months has been shown to be effective in preventing symptomatic vulvovaginal candidiasis, and use of an individualized, decreasing regimen can lead to efficient prevention of recurrence in the long term.

How To Reduce Pain in Vulvodynia

Peripheral Nociceptive Blockade and Central Inhibition

Transcutaneous electrical nerve stimulation (TENS) is a technique that provides neuromodulation via an electrical stimulus. It was originally developed in the early 1970s as a screening technique for the selection of women with chronic pain most likely to achieve satisfactory pain relief by implant of an electrical stimulator. The management of chronic pain such as in chronic neuropathies, postherpetic neuralgia and trigeminal neuralgia by TENS is supported by a large number of clinical trials. It has been demonstrated that TENS is of significant benefit in the management of vestibulodynia, but it is essential to use appropriate and validated stimulation parameters.

TENS treatment can be self-administered in the privacy of a woman's home after a short period of supervision, using an inexpensive device. Our experience with a large series of provoked vestibulodynia patients (480 women) showed that there is a positive response after 10 to 15 sessions (symptom reduction >50%) which tends to peak after 25 to 35 sessions. A 65-75% response rate to TENS for provoked vestibulodynia has been reported.

Box 4. The use of TENS in the treatment of vestibulodynia

Potential mechanisms for its effectiveness include:

- 'Pain gate control', that is, blocking the information travelling along the nociceptive fibers through stimulation of the large diameter afferent Ab fibers
- 'Extrasegmental action', based on the release of endogenous opioids by stimulation of small diameter afferent and motor fibers

Stimulation is delivered via a vaginal probe 20 mm in diameter and 110 mm in length, with two gold metallic transversal rings as electrodes. It should be inserted into the vagina up to 20 mm.

The nociceptive system is best suited to the new situation through a gradual increasing of day numbers between TENS sessions.

Oral Agents

A survey of clinicians has indicated that oral medications are more likely to be used for the treatment of generalized vulvodynia than for provoked vestibulodynia.

Trycyclic antidepressant (TCAs) are an appropriate pharmacological management option in the treatment of vulvodynia, in particular for unprovoked and generalized pain. Originally used to treat depression, this class of medication is now commonly prescribed to treat chronic pain. Amitriptyline is the most commonly used TCA for this indication. Amitriptyline should be started at a low dose, with slow titration until either the patient responds or has unacceptable side effects. Furthermore it cannot be abruptly stopped and needs to be tapered according to the side effects. Side effects in some patients might influence compliance with treatment to a level that can cause withdrawal.

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Side effects of TCA treatment should be discussed with the patient. Common side effects are: fatigue, dry mouth, weight gain, constipation; occasionally, cardiac and arrhythmic effects can occur, so TCAs should be used with caution in the elderly.

A 47% complete response rate to TCAs for unprovoked vulvar pain has been reported.

Box 5. Trycyclic antidepressant (TCAs)

- Amitriptyline is the most widely used TCA in vulvodynia patients
- Start with a low dosage and slowly increase—10 mg tab
- Increase in steps of 5 mg, as tolerated, every 3-7 days up to 125-150 mg
- The average dosage is 60 mg daily
- Dose should be taken at approximately at 1-2 hours before bedtime to help counteract morning sedation and fatigue

Serotonin-norepinephrine reuptake inhibitors (SNRIs, such as *v*enlafaxine and duloxetine*)* have proven to be effective in neuropathic pain, but have not been well studied in vulvar pain. The best results for pain are achieved with daily doses of venlafaxine 225 mg and duloxetine 60 mg.

The strength of the pain-relieving action of SNRIs is lower than that of tricyclic antidepressants, with a combined NNT (number-needed-to-treat) value in painful neuropathies of about 5 for the two SNRIs and 2.3 for tricyclic antidepressants. Indeed, for this very reason, the European Federation of Neurological Societies guidelines recommend SNRIs as second-line treatment.

Other drugs that can be used in vulvodynia patients are gabapentin and pregabalin. Gabapentin is an antiepileptic medication that is now indicated for the treatment of chronic pain. Although pregabalin has a mechanistically similar action to gabapentin and shares similar advantages, such as a lack of pharmacokinetic interactions with other medications or enzyme induction, there are several differences between the two drugs.

Unlike gabapentin, pregabalin exhibits linear pharmacokinetics after oral administration, with low intersubject variability. This provides a more predictable dose-response relationship, because plasma concentrations increase linearly with increasing dose. Gabapentin requires disproportionately larger dosage increases to achieve increases in plasma concentrations. The large doses required for some patients receiving gabapentin could worsen dose-dependent adverse effects, such as dizziness and som-

nolence. The linear pharmacokinetics of pregabalin impart a better-defined effective dosage range and may provide the basis for the efficacy of either fixed- or flexible-dosage regimens.

Despite these preclinical data, it is unclear if pregabalin has a clinical advantage over gabapentin, as the two drugs have not been compared in clinical trials. It has been reported that 64% of women with generalized vulvodynia had resolution of least 80% of their symptoms. Although no specific studies in vulvodynia have yet been conducted, one case report indicated that pregabalin is successful in managing the pain of generalized vulvodynia.

Box 6. Gabapentin and Pregabalin

- Gabapentin can be started at 100 mg and then slowly increased to bid, then tid-gabapentin is slowly increased by 100 mg at each dose. The maximum recommended dose is 3200 mg daily
- Pregabalin can be started at 25 mg twice daily and may be increased to 75 mg daily within two weeks based on efficacy and tolerability
- Adverse effects : dizziness (8-43%); somnolence (6-30%), weight gain (5-20%), peripheral edema (3-19%) and diplopia (2-13%)

Amytriptiline drop formulation allows an easy, slow titration (1 drop = 2 mg).
Combination therapy should preferably use drugs with complementary mechanisms.
The synergistic interactions between antidepressants and gabapentin/pregabalin, for example, are not only logical but also encouraged by a reduction of side effects by the use of lower doses.

Trigger Point Injection

The use of injectable therapy in the management of vestibulodynia can be useful, in selected patients, the main objective being the inactivation of the trigger point, thereby reducing pain. The therapy should be used in combination with other approaches as a complementary treatment or like treatment of a residual disease.

Various combinations of drugs have been suggested, but we currently think that only two regimens should be used: corticosteroid *plus* anesthetics and botulinum toxin (see section on pelvic floor dysfunction) (Table 8.1).

Table 8.1 Trigger point injection

Corticosteroid plus anesthetics Methylprednisolone and lidocaine	Botulinum toxin Botulinum toxin type A
Rationale: - Corticosteroid act via inflammatory/ cytokine alterations (decreased numbers of mast cells degranulated)	**Rationale:** - Inhibition of pelvic floor hypertonicity: injection into the pelvic floor muscles
- Anesthetic agents act by blocking sodium channels and can be effectively used for pain modulation at low doses that do not block complete nerve impulse propagation	- Direct anti-nociceptive effect: injection in painful area of vestibular epithelium
Characteristics of patients eligible for therapy: - Patients with dyspareunia (provoked pain)	**Characteristics of patients eligible for therapy:** - Patients with dyspareunia (provoked pain)
- Pain *only* with sub urethral localization and very *localized* (two or three sites)	- Patients with associated pelvic floor dysfunction

Pudendal Nerve Block

The use of pudendal nerve block (Fig. 8.1) for treating pudendal neuralgia is a technique widely used by neurologists and anesthesiologists. Patients with pudendal neuralgia tend to describe neuropathic pain symptoms in the nerve's distribution. We think that there is not a substantial difference between generalized vulvodynia and pudendal neuralgia, so that pudendal nerve block can be a possible therapy in patients with generalized vulvodynia (Table 8.2).

Table 8.2 Pudendal neuralgia versus generalized vulvodynia

	Pudendal neuralgia	Generalized vulvodynia
Mean age of presentation	Sixth decade of life	Postmenopausal women
Definition	Pain involving the sensory distribution of pudendal nerve	Symptoms anywhere within the distribution of the pudendal nerve
Presentation	Pain is generally constant and it may be exacerbated with sitting and diminished by standing	Symptoms are unprovoked and worsen with provocation, although the pain pattern is highly individualized

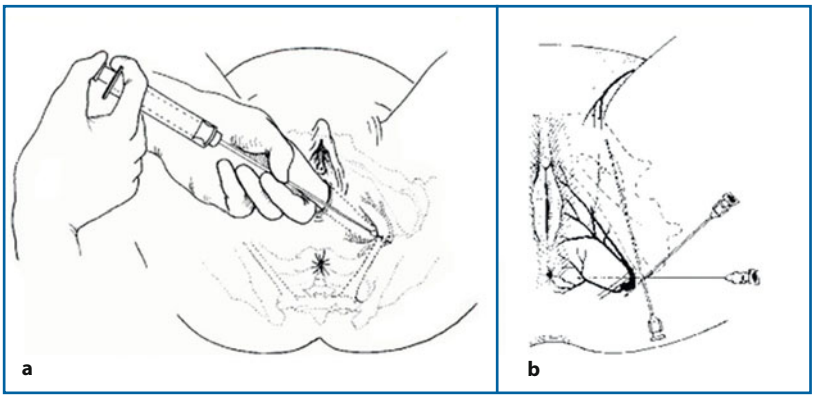

Fig. 8.1 **a** The palpating finger is used to locate the ischial spine and sacrospinous ligament per vaginam. The needle is inserted through the vaginal wall, is directed towards the spine and then passed through the sacrospinous ligament. As soon as the needle has passed through the ligament, a loss of resistance is felt. **b** The perineal approach to pudendal nerve block

The most widely used protocol is local anesthetic and sometimes corticosteroid injection performed at three levels, two at the ischial spine level and one at Alcock's canal. There is no consensus on the maximum number of nerve blocks that should be given, and despite it was reported a response rate about 60% the long-term response effects are unknown. Various pudendal nerve block approaches have been described via different routes: transvaginal, transperineal and transgluteal. The main problem associated with these approaches is the risk for the patient, as this is a blind technique in a vascularized region close to the bowel and bladder. However, the approach can be guided by different imaging technique utilizing fluoroscopy or computed tomography.

Surgery

Surgical excision of the vestibule may be considered in patients with local provoked vulvodynia (vestibulodynia) after other non-surgical measures have been tried. The procedure that yields the best result is modified vestibulectomy in which a horseshoe-shaped area of the vestibule and inner labial fold is excised, followed by advancement of the posterior vaginal wall (Fig. 8.2).

Surgical success rates range from 40% to 100%, with success defined as much improved or completely cured. Factors that limit direct comparison are differences in numbers of patients, presence of associated comorbidities

such as painful bladder syndrome, other medical treatment at the time of surgery, the technique used, definition of success, and length of follow-up. Nevertheless, the 70% average success rate for surgery makes it a therapeutic approach to consider for this debilitating condition. First and foremost, however, patient selection is crucial. In addition, adequate counseling and support should be given to the patient both pre- and postoperatively.

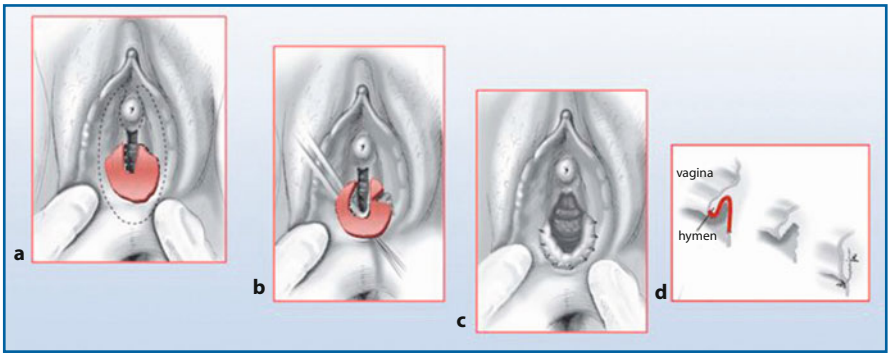

Fig. 8.2 a-d The procedure consists of an excision of a U-shaped area of the posterior vestibule up to the inner aspect of the labia minora and the lower portion of the hymenal ring, according to the marking. The thinnest possible tissue section was removed and sent for pathological examination. The vaginal epithelium was pulled out and attached to the skin of the perineum, replacing the excised area by interrupted dissolving sutures and the retain hymen is used as a flap

Box 7. Surgical therapy for vulvodynia

Predictors of surgical failure:

- Diffuse and unprovoked vulvar pain, urinary symptoms, and muscle hypertonicity

Predictors for a successful outcome:

- Provoked vestibular pain (dyspareunia), fewer sites of pain, relatively young age

Complications of surgery:

- Short-term: bleeding, infection, hematoma and partial wound separation
- Long-term: Bartholin duct cyst (2-6%), enhanced vestibular tenderness (5%)

Action Towards Associated Pelvic Floor Dysfunction

There are many beneficial measures to help relax the pelvic floor muscles. Physical therapy is effective in lowering pelvic floor hypertonus and a variety of techniques, including pelvic floor exercises, external and internal soft tissue self-massage, trigger point pressure, biofeedback and use of vaginal trainers, can be used. Often patients have no awareness of their pelvic floor and instructing them to 'check' their pelvic floor tension throughout the day is helpful in their understanding of the the importance of keeping the pelvic floor relaxed. Biofeedback techniques are key to attaining this target.

With a vaginal probe, levator ani activity can be monitored by the patient and her therapist, and with careful coaching the patient can be taught how to contract and then relax her pelvic floor using various protocols. Generally the goal is to teach muscle awareness and relaxation.

Typically sessions last 20 to 30 minutes and a success rate in the 60-80% has been reported.

Manual therapy techniques are especially important for patients with myofascial pain disorders and include myofascial release, trigger point release, soft tissue mobilization, and massage. These internal techniques can be complemented by the patient being educated in the use of *vaginal dilators* for self massage.

Sexual partners should also be educated in these techniques in order to encourage and provide further supportive therapy at home. The presence of the dilator provides propioception to the musculature during exercise, augmenting improved pelvic floor contraction and relaxation. Vaginal dilatation can also diminish the anxiety associated with penetration as the woman has complete control of vaginal entry.

Botulinum neurotoxin (BoNT): The primary mode of action of BoNT is chemodenervation of muscle via blockade of presynaptic acetylcholine release at the neuromuscular junction, with subsequent paralysis. In therapeutic use, BoNT has also demonstrated effectiveness in the treatment of pelvic pain disorders characterized by functional abnormalities of muscle tension and relaxation, such as vaginismus. BoNT can be injected into the bulbospongiosus and pubococcygeus muscles. The majority of studies of BoNT in vulvar pain syndrome are targeted at pelvic floor spasm or inhibition of muscle spasticity. These trials represent some optimistic preliminary data that warrants further research in order to standardize dosing and optimize the number of injections.

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Box 8. Pelvic floor rehabilitation

- EMG Biofeedback
- Myofascial release: manual therapy technique that use light stretch to restore myofascial mobility and muscle length
- Myofascial trigger points release. Manual therapies used to eliminate trigger points include skin rolling, strumming and stripping of the affected muscle fibers

Typically, pelvic floor dysfunction must be treated as part of a multimodal treatment plan and a physical therapist with experience in vulvodynia needs to be involved in the interdisciplinary treatment of the disease.

Action Towards Psychosexual Ramification of the Syndrome

Vulvar pain has physical, psychological and relationship aspects. Patients with localized and generalized vulvar pain need varying degrees of sexual counseling and emotional support.

Sexual dysfunction as predisposing/precipitating/maintaining factors contributing to vulvodynia should be investigated, including physical or sexual abuse, or adverse life experiences (e.g., parental divorce, pregnancy termination, difficult childbirth). Because living with chronic genital pain often has psychosexual consequences, some women may benefit from adjunct counseling or sex therapy. Cognitive-behavioral therapy is a useful psychological approach to reduce vulvar pain and improve sexual function.

It is important to keep in mind that decreasing dyspareunia does not necessarily lead to a restoration of sexual function, especially in women with long-term vulvodynia. In these cases sex therapy, couples counseling, psychotherapy, or a combination is often very helpful.

Case Studies

Case Study: "Julie"

- A 31-year-old, nulliparous woman;
- comfortable with intercourse until 3 years ago when she was treated for a severe bladder infection. Antibiotics precipitated a yeast infection, for which she was also treated;
- she complains of dyspareunia, with stinging and burning pain in the vestibule during and after intercourse;
- she has had increasing pain with intercourse, to the point that she has had to stop having sex.

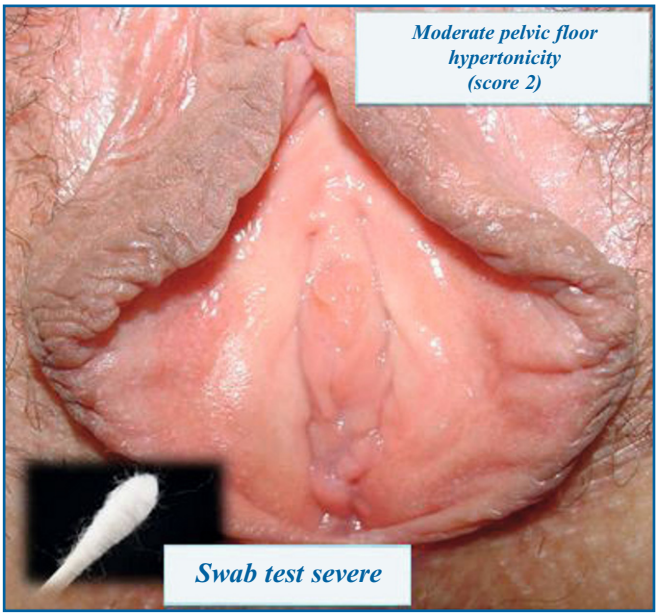

Fig. 8.3 Physical findings of the patient

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Diagnosis

Provoked vestibulodynia

A therapeutic program for this patient can be structured as follows:

Vulvar care measures to minimize vulvar irritation	This is a first therapeutic approach that should be applied to any patient suffering from vulvodynia, regardless of the disease subtype
Reduction of triggering stimuli	- It is useful to use a preventive treatment for recurrent yeast infection with fluconazole (150-200 mg weekly for 1-2 months) - Postcoital antibiotic prophylaxis (ciprofloxacin 250 mg or levoxacin 200 mg within 20-30 mins after sexual intercourse) can be used to prevent post-coital urinary tract infections
TENS + Pelvic floor rehabilitation	Pelvic floor rehabilitation cannot be used if the pelvic floor hypertonicity score is 0 or 1, in fact the TENS pain reduction can resolve the alterations of pelvic muscles

After 15-20 TENS + pelvic floor rehabilitation
Julie's condition improved (dyspareunia score is 1)
but it is not fully resolved

Trigger point injection	Vestibular infiltration of methylprednisolone and lidocaine or Botulin Toxin A can help to resolve a very localized residual disease
Psychosexual counseling	In many patients sex has been painful for a long time or the woman has not had sex for a long time due to the pain. As a result, she may have developed negative feelings towards sex, or possibly her relationship with her partner Psychological support, for this reason, can play an important role

Case Study: "Sally"

- 53-year-old female;
- complains of chronic pain in the vulvar region of 4 years' duration;
- the pain first began as discomfort in the vulvar region of moderate intensity, accompanied by painful burning and stinging sensations;
- pain was initially intermittent in nature, lasting for about 2 days per episode;
- the patient received hormone treatment and corticosteroids without any improvement of symptoms;
- one year after the start of vaginal discomfort, the pain became constant and diffuse in nature and was now characterized as a constant burning sensation with increased sensitivity to tactile stimuli;
- the patient rated the pain as 7 out of 10 in intensity on the visual analogue scale (VAS) for pain and was now unable to wear tight-fitting underwear;
- there was moderate improvement with analgesic drugs, and the patient described light relief of symptoms when lying down (VAS:3).

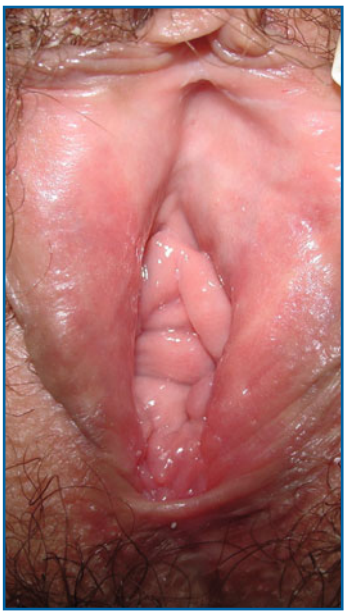

Fig. 8.4 Gynecologic examination, including vulvoscopy, revealed no abnormalities

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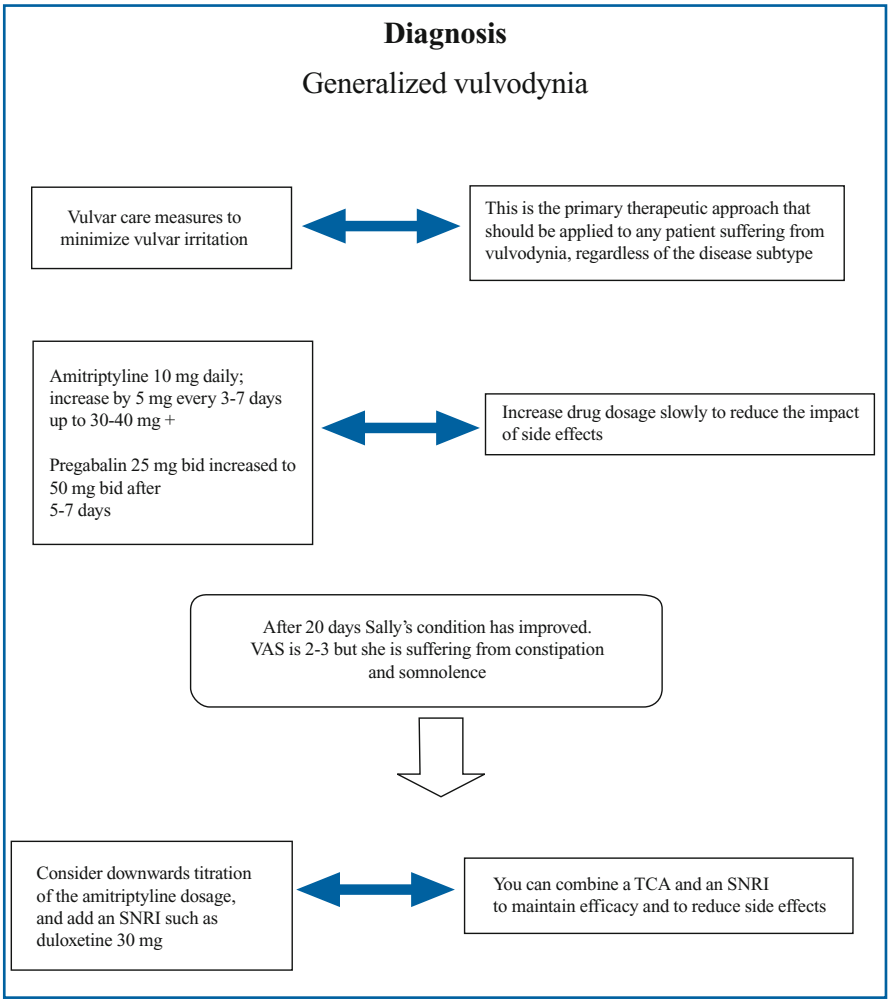
Diagnosis
Generalized vulvodynia
Vulvar care measures to minimize vulvar irritation
This is the primary therapeutic approach that should be applied to any patient suffering from vulvodynia, regardless of the disease subtype
Amitriptyline 10 mg daily; increase by 5 mg every 3-7 days up to 30-40 mg +
Pregabalin 25 mg bid increased to 50 mg bid after 5-7 days
Increase drug dosage slowly to reduce the impact of side effects
After 20 days Sally's condition has improved. VAS is 2-3 but she is suffering from constipation and somnolence
Consider downwards titration of the amitriptyline dosage, and add an SNRI such as duloxetine 30 mg
You can combine a TCA and an SNRI to maintain efficacy and to reduce side effects

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