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A principal pathogenic mechanism in dyspareunia is altered **awareness of pain recurrence due to previous experiences of coital pain**.

Therefore, the focus during sexual intercourse turns to **sensation of (possible) pain instead of enjoyment**

The experience of pain and the loss of pleasure are recurrently recognized and become reinforced by repeated experiences. This process creates a cognitive scheme of negative expectations that disturbs sexuality

Consequently, responses to dyspareunia include **starting but then stopping intercourse**, **changing positions**, **enduring intercourse because of a desire for pregnancy**, and **enduring intercourse because of a reluctance to allow endometriosis to affect yet another aspect of life** or because **of a desire for closeness with a partner**

They cope with pain, either because their **wish for a pregnancy outweighs their experience of pain** or because of the importance of **sexual intimacy**.

- Knowing that sexual desire is profoundly influenced **by emotion and it is governed by a complex of inhibitory and excitatory influences**, studies reported lack of sexual desire in 45 % of women with deep infiltrating endometriosis, in spite of 14 % of healthy women.
- Orgasm and satisfaction, as aspects of sexual function, are also impaired in women with endometriosis. They have a multifactorial genesis depending on psychological, anatomic, and physiological factors.
- Due to their awareness of feeling pain, women with endometriosis may develop an unrelaxed attitude through the intercourse, and they hardly achieve orgasms compared to healthy women.
- Anticipation and fear of pain may provoke **decreased arousal**; **lack of lubrication**; **pelvic floor hypertonus**, **resulting in mechanical trauma of the vestibular mucosa and urethral meatus**; as well as resistance to penetration due to restriction of vaginal entry

In endometriosis patients, the mechanism of pain during coital activity can be caused by:

traction of the inelastic parametria

by pressure on the endometriotic nodules

by immobilization of postero-uterine pelvic structures,

and by a neuropathic mechanism related to nerve injury or inflammatory stimuli.

The presence of endometriosis is associated with an **increased pain perception**, and women with endometriosis generally experience major exacerbation of pain when even minor pressure is exerted on nodules

- **Hyperalgesia** is the occurrence of excruciating pain when a non-painful stimulus is applied and is a foremost characteristic of neuropathic pain, which corresponds to a painful sensation that is out of proportion with the intensity of nociceptor stimulation.
- **Neuropathic** pain is usually related to nerve injury or inflammatory stimuli.
- Both of these conditions are found in endometriosis, as it has been demonstrated that sensory nerve fibers are frequently invaded by endometriotic stromal cells and that several mediators such as histamine, tryptase, tumor necrosis factor α, prostaglandins, serotonin, interleukin-1, and nerve growth factor are abnormally synthesized and released by activated macrophages and mast cells as well as leukocytes within the endometriotic lesions, around sensory nerve fibers, and in peritoneal fluid.
- Based on the chronic inflammatory condition primed by ectopic endometrium, a sort of vicious cycle may develop that determines nociceptors, sensitization, neurotropism and local neoneurogenesis, and activation of sensory nerve fibers, with resulting hyperalgesia
- Moreover, there is evidence that the presence of endometriosis is associated with increased pain perception , due to abnormal modulation of nociceptive input with an increase in the intensity of the neural signal ascending to the cerebral cortex
- Therefore, pain originating in endometriotic foci appears to lead to central sensitization and generalized hypersensitivity
- Organic problems may cause also secondary sexual dysfunction, as factors responsible for the origination of pain may be different from the ones that are active in the perpetuation of pain .
- Thus deep dyspareunia caused by endometriosis can be viewed as an originally visceral type of pain secondary to chronic inflammation but with several superimposed components, including hyperalgesia, abnormal cortical perception, and psychological factors

Endometriosis: Types and Sexual Function

Endometriosis is classified in different anatomical types such as:

Superficial

Ovarian

and deep infiltrating endometriosis (DIE).

It is estimated that the incidence of DIE is around 20 % of women with endometriosis .

There is a substantial impact of endometriosis on the quality of sex life: between 33.5 % and 71 % of women reported that endometriosis negatively affected their sex lives.

It was reported that quality of sex life was affected in all stages of endometriosis both in women with minimal and severe endometriosis .

Dyspareunia was reported in 67 % of women with rectovaginal endometriosis, 53 % of women with peritoneal and/or ovarian endometriosis, and in 26 % of controls. No differences in sexual function were found between women with diverse endometriosis forms

- In particular, DIE defined as a form of endometriosis which penetrates for more than 5 mm under the peritoneal surface is strongly associated with a significant reduction of quality of life and sexual function
- It involves the uterosacral ligaments, vagina, intestinal wall, rectovaginal pouch, ureteral, and urinary bladder
- Several studies correlated dyspareunia with the presence of DIE specifically of the uterosacral ligaments
- Similarly, the presence of a vaginal nodule may affect sexual function through its direct stimulation during intercourse
- In general, nociceptive input from viscera, either the vagina or uterosacral ligaments affected by endometriotic lesions, leads to a central sensitization and provokes a generalized hypersensitivity in women with this disease

  studies demonstrated that complete excision of endometriosis, including vaginal lesion resection, seems to offer a significant increase in sexual satisfaction and decrease in sexual problems .

  Moreover, advanced stage of disease may affect several aspects of women's life including psychological areas, and it seems that the number of deep infiltrating endometriotic nodules is directly proportional to the reduction of sexual function .

  Three potential predictors (pelvic pain intensity, DIE status, and revised American Society for Reproductive Medicine stages) of female sexual dysfunction were identified in women with histologically confirmed endometriosis. The multivariable analysis showed that moderate-to-severe pelvic pain and revised American Society for Reproductive Medicine stage III or IV were associated with increased risk of having female sexual dysfunction

  Stages 1 & 2 (minimal to mild disease): Superficial peritoneal endometriosis. Possible presence of small deep lesions. No endometrioma. Mild filmy adhesions, if present.

  Stages 3 and 4 (moderate to severe disease): The presence of superficial peritoneal endometriosis, deeply invasive endometriosis with moderate to extensive adhesions between the uterus and bowels and/or endometrioma cysts with moderate to extensive adhesions involving the ovaries and tubes.

  Women with the rectovaginal endometriosis had more than three times the risk of being sexually unsatisfied or feeling little or no sexual pleasure and about two times the risk of engaging in limited or no sexual activity and of reduced capacity to reach orgasm, compared with patients without endometriosis.

  However, subtle differences in frequency and severity of deep dyspareunia between women with rectovaginal lesions and those with peritoneal and/or ovarian lesions were found.

  There was a lack of correlation between severity of deep dyspareunia and level of sexual functioning in patients with endometriosis, independently from lesion type. Probably, the relationship between endometriosis and sexual dysfunction is much more complex than can be explained by anatomic distribution of lesions. A possible explanation is that organic

dyspareunia is just one among a number of determinants of sexual functioning in women with endometriosis.

In other words, because female sexuality is multifactorial and comprises psychologic processes, the effect of pain at intercourse could have been buffered or diluted by other factors, thus reducing part of its relative impact.

Personality traits, coping capacity, degree of couple intimacy, partner emotional support, participation, solicitousness or hostility, marital adjustment, and even quality of medical information and care may greatly influence the level of perception, interpretation, and acceptance of such a multifaceted symptom

- In conclusion, independently from lesion type, women with endometriosis reported more frequent and severe deep dyspareunia and performed worse in terms of sexual functioning compared with women without endometriosis. Owing to the intimate nature of the symptom, dyspareunia should be viewed in a broader clinical perspective, considering also the potential psychologic and interpersonal consequences.
- In other words, dyspareunia should not be simplistically considered to be equivalent to any other organic pain symptom, but should instead be investigated within the context of relational adjustment, psychologic well-being, global sexual functioning, and overall female health

Endometriosis and Psychological Impact on Relationship

- the experience of living with endometriosis disrupted day-to-day life and intimate relatedness for couples. there are five identified relationship "coping" patterns:
    - "together but alone,"
    - "battling together,"
    - "conjoined through disability,"
    - "totalized by care giving,"
    - and "engaged in mutual care"
- Partners of women with endometriosis should be intensely involved in the management of the disease from the beginning.
- Proper counseling of the woman and her partner on the nature of the disease and its potential consequences for their sex life could hopefully diminish the sexual burden for these couples.
- Qualitative research found that women were reluctant to discuss dyspareunia with healthcare professionals and that women reported that healthcare professionals did not ask about this
- The weight of evidence from quantitative studies suggests that rates of depression, anxiety, and emotional distress are higher for women with endometriosis than control groups or the general population.

- While no firm conclusions can be drawn about the role of pain when comparing women with endometriosis pain and women with pain-free endometriosis, the overall findings comparing women with chronic pelvic pain related to endometriosis and women with chronic pelvic pain from other or unknown causes suggest that it is the experience of pain that is associated with mental health difficulties and emotional distress.
- Qualitative studies highlight the emotional distress that characterizes many women's lives, including feelings of isolation, guilt, worry, worthlessness, and hopelessness and feeling unable to cope.
- The mechanisms by which this occurs are unclear however, as pain, emotional distress, fatigue, and dissatisfaction with healthcare and available treatments are all interwoven within the complex experience of endometriosis. Despite calls for care and support to better focus on psychological and emotional experiences and impact, depression, anxiety, and emotional distress appear to prevail, and there are few reports of systematic interventions to address these issues.

Clinical and Demographic Factors and Sexual Function

- A prospective cohort study evaluated the impact of sociodemographic and anamnestic characteristics of women with deep infiltrating endometriosis on the quality of life and sexual function.
- A poor quality of life and sexual function were found which were worsened by the presence of history of previous surgery and low BMI. Probably the adipose tissue, by producing estrogen, may positively influence the sexual life through an increase of libido and sexual desire.
- In a previous study, it was reported that a high BMI was associated with a longer delay in the time of diagnosis compared to patients with low BMI. This may, in part, be explained by the fact that overweight women had less sexual dysfunction than normal-weight women.
- Another important aspect is represented by infertility together with depression, is highly prevalent in women with endometriosis, and is also associated with the impairment of sexual function
- It can cause psychological changes, such as anxiety that might negatively affect physical and emotional health, quality of life, and sexual function. Limited research suggests that the impact, or potential impact, of endometriosis on fertility causes worry, depression, and feelings of inadequacy.
- Previous studies have demonstrated that infertility is associated with difficulties in interpersonal relations and social interactions, impaired dyadic relations, reduced self-esteem , feelings of shame , social isolation , and compromise mental health .
- Emotional problems increase with the duration of infertility and with advancing age in women as their childless years increase
- It should be noted that reduced sexual desire and sexual intercourse frequency may occur due to the loss of sexual spontaneity that is secondary to certain strategies used to increase the chances of pregnancy.

- Depressive symptoms are usually associated with changes in sexual function such as reduced sexual satisfaction, dysfunction of excitement, and less pleasure during sexual relations .
- Contrary, a study reported that infertile females had better partner relationships than fertile females, and demonstrated that several unsuccessful attempts at treatment of infertility were associated with good dyadic consensus and cohesion.
- It is possible that partners become more supportive by sharing the stressful experiences associated with treatment of infertility, and this may improve the marital relationship and increase dyadic cohesion. Considering that almost half of infertile women have endometriosis, further researches into the social and psychological experience of infertility are necessary among women with endometriosis.

Medical Management of Endometriosis and Sexuality

- Medical treatments are effective in decreasing pain with intercourse.
- Several pharmacological compounds have been used successfully in women with deep dyspareunia associated with infiltrating endometriosis, including depot intramuscular GnRH agonists, vaginal danazol, oral aromatase inhibitors, progestins directly delivered into the uterine cavity, and oral, intravaginal, transdermal estrogen–progestogencombinations as well as oral progestogens alone.
- In a randomized controlled trial, a GnRH agonist was more effective than an estrogen–progestin on pain at intercourse, and the combination of low-dose norethisterone acetate with an aromatase inhibitor (letrozole) reduced deep dyspareunia to a larger extent than low-dose norethisterone acetate alone in women with rectovaginal endometriosis
- the effect of laparoscopic treatment versus low-dose norethisterone acetate for the management of severe deep dyspareunia associated with persistent or recurrent endometriosis after unsuccessful first-line conservative surgery.
- Authors reported a rapid improvement of sexual functioning and psychological status after surgery but worsened with time, whereas the effect during progestin use increased more gradually and progressively without overall significant differences between the groups at 12-month follow-up.
- Both surgery and medical treatment with progestins resulted valuable options for improving the impact of dyspareunia on sexual function and quality of life . However, hormonal treatments fail in approximately 1 woman out of 3, are associated with a high recurrence rate after discontinuation, cannot be used in women seeking conception as they inhibit ovulation, and may interfere with sexual desire and arousal

Surgical Management of Endometriosis and Sexuality

- Dyspareunia, especially deep dyspareunia, is present in 60–80 % of patients who undergo surgery for endometriosis and 50–90 % of those receiving conservative treatment for the condition
- Several studies have demonstrated that surgical excision of deep endometriotic lesions markedly reduces the severity of dyspareunia
- and improves the quality of sexual function in these patients. Excision of endometriotic foci has been reported to be effective in reducing pain at intercourse and in ameliorating quality

of sex life, but surgery for deep lesions requires a high level of technical competence, is associated with potentially severe morbidity, and generally results in only partial or temporary efficacy

- It was suggested that women treated for deep infiltrating endometriosis, after surgery, managed to relax and feel more comfortable during intercourse because of the reduction of pain symptoms and the awareness of the removal of endometriotic lesions.
- Moreover, the complete excision of all endometriotic lesions and the restoration of normal pelvic anatomy might reduce interference with sex by pelvic problems.
- A positive correlation seems to exist between the extent of endometriosis resection and the degree of postoperative symptom improvement.
- Garry et al. observed that the excision of endometriotic lesions significantly improved quality of sexual function at 4-month follow-up.
- Ferrero et al. observed a significant improvement in sexual life at 6-month and 12-month follow-up after surgical excision of DIE.
- Patients had increased variety in sexual life, frequency of intercourse, more satisfying orgasms with sex, and relaxed easier during sex and were more fulfilled after sex
- However, the effect of surgery is generally partial or temporary.
- Vercellini et al. in a prospective cohort study demonstrated that surgery and low-dose progestin therapy are both effective in improving sexual functioning, psychological well-being, and health-related quality of life in women with endometriosis-associated deep dyspareunia, although with a different chronological pattern.
- Excision of lesions is followed by a rapid and substantial benefit, with a greater immediate effect with respect to progestin treatment. However, the gradual recurrence of pain at intercourse after 6 months since surgery, combined with progressive amelioration of clinical conditionsin women using low-dose progestin therapy, leads to a final practical equipoise in the considered functional outcomes at 1-year follow-up. Moreover, the mean total Female Sexual Functioning Index score never exceeded the “normality” cutoff limit of 26.55 at any time point
- Therefore, the sexual dysfunction observed at baseline was completely corrected neither by surgery nor by medical treatment.
- In particular, performance in the surgery group improved substantially in the short term and then gradually deteriorated. However, at 12 months of evaluation, desire, arousal, and lubrication scores were still significantly higher than in the low-dose progestin therapy group, resulting in a tendency toward better total FSFI score after surgery.
- Probably medical therapy induces a decreased desire, arousal, and lubrication, but once intercourse initiates, orgasm capacity and overall satisfaction are not worse than in the surgical group. Conversely, 1 year after surgery, women maintained an unaffected sexual predisposition, but experienced slightly more pain during intercourse.
- As Ferrero et al. reported, the best results in reduction of pain at intercourse with an improvement in quality of sex life can be obtained with surgery, followed by postoperative medical treatment; thus there is an increasing consensus among experts in endometriosis

that hormonal therapies should be systematically proposed to women who do not intend to conceive. Postoperative medical treatment reduces the risk of recurrence inducing the atrophy of the eutopic and ectopic endometrium.

- Combination of surgery, followed by medical treatment of DIE, was also proven to improve symptoms and quality of life
- Women after surgery for bowel endometriosis (with and without bowel resection and reanastomosis) had improved levels of depression, relationship satisfaction, and sexual functioning. Patients with bowel resection had significantly better outcomes
- in the proportion of women with depressive symptoms as well as lower levels of sexual problems with orgasm and pain during intercourse than patients without.
- However, it is possible that women with bowel resection experience a greater difference in depression, relationship satisfaction, and sexual functioning after surgery because of the more severe situation before surgery. The extensive surgery of bowel resection gives patients experience of more intensive follow-up due to the nature of their surgery, and this may turn in reduced level of depression
- However, laparoscopic management of DIE is a complex surgical procedure, which may be complicated by neurogenic impairment of urinary, intestinal, and sexual function, especially in cases where nerve-sparing surgery is not feasible.
- Complete DIE lesion resection can cause postoperative dysfunction of the genitals, bladder, and bowel, although pain symptoms are greatly alleviated.
- During dissection of the rectum and uterosacral ligaments, autonomic nerves supplying the rectum and urinary bladder may be damaged leading to urinary, defecatory, and sexual dysfunction. The problem is well recognized, and a nerve-sparing bowel resection technique for endometriosis has been introduced in order to avoid autonomic dysfunctions.
- Recently, studies have shown that nerve-sparing surgery for DIE can reduce bowel and bladder dysfunction without decreasing surgical efficacy. During this surgical procedure, the branches of the inferior hypogastric nerves that supply the bladder, colon, cervix, and vagina are identified and preserved, whereas DIE lesions are excised.
- the total FSFI score and the sub-score for each of the six domains in patients with nerve-sparing surgery or conventional surgery for DIE were below the clinical cutoff scores before surgery, and these scores significantly increased after surgery.
- These findings suggest that sexual dysfunction is reduced by surgery but not by the nerve-sparing technique. The tendency to increased pain symptoms and sexual dysfunction over time after operation may be caused by new DIE lesions or remaining DIE lesions which are caused by incomplete excision during the surgical procedure
- Moreover, besides the risk of autonomic nerve injuries, aggressive surgery such as bowel resections and resection of large parts of the uterosacral ligaments with consequent scarring of the pouch of Douglas can adversely contribute to an impaired sex life. Women should therefore always be counseled appropriately prior to surgery so that they are aware of these potential risks.

- Furthermore, advice should be heeded from the recently published consensus on the current management of endometriosis that those women with a higher stage of disease and/or intractable clinical problems should receive care from a center of expertise with appropriate surgical expertise in the laparoscopic excision of endometriosis
- In conclusion, considering the multidimensional impact of endometriosis, the treatment approach should include emotional and social support, stress reduction, psychosexual treatment, and a focus on quality of life issues, sex and relationships, pain management, and career counseling
- Psychological and psychosexual counseling should be offered when dealing with endometriosis patients and should be an essential component of endometriosis treatment.
- It is very important that gynecologists involved in the management of endometriosis offer patients a profound conversation about their sexuality, because these professionals in most cases are the first reference persons for suffering women. Due to the fact that sexuality, especially impaired sexuality, is often a shameful topic, it is the task of the gynecologists to address this delicate issue in a pleasant way.
- The World Health Organization has included sexual health among human rights, and the report of a technical consultation on sexual health held in Genova (2002) states that “sexual rights embrace human rights, including the right of all persons to pursue a satisfying, safe, and pleasurable sexual life.”
- Dyspareunia should not be simplistically considered equivalent to any other organic pain symptom but should instead be considered within the context of global sexual functioning, relational adjustment, psychological well-being, and overall female health.