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Menopause and sexuality: key issues in premature menopause and beyond

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Abstract

Woman's sexuality encompasses sexual identity, sexual function, and sexual relationships. It is modulated throughout life by life and reproduction-related events, health, relationships, and socio-cultural variables. The ageing process and menopause are two potent contributors of female sexual dysfunction. The earlier the menopause, the more severe and complex the impact on sexuality is. The younger the woman, the less she realizes the different key goals of her life cycle (falling in love, having a satisfying sexual life, forming a stable couple, getting married, having a family) and the more pervasive the consequences on her sexual identity, sexual function, and sexual relationship can be. Premature menopause is an amplified paradigm of the complex impact menopause can have on women's and couple's sexuality. The paper will focus on biologically based sexual issues, namely desire, arousal, orgasm and pain disorders, as well as key questions encountered in infertility. The concepts of "symptom inducer" and "symptom carrier" will also be addressed.

Introduction

Woman's sexuality encompasses sexual identity, sexual function and sexual relationships. It is modulated throughout life by a number of factors, including life events, reproduction-related events, health, relationships, and socio-cultural variables.[1] Sexuality, as part of human behavior, is a complex phenomenon that receives physiological and psychological influences. For this reason the definition, prevalence, assessment, and evaluation of its disorders have been traditionally difficult. [2]

Female sexual dysfunction can occur at any age but is most common around mid-ages. Two important overlapping factors that affect female sexuality are the ageing process and menopause. Sexual problems can be a particularly important facet of the menopausal transition and are more likely to be a cause of concern if the hormone deficiency is ultimately responsible.

Unfortunately, women are never too young to become menopausal, especially when menopause is the result of either a spontaneous or iatrogenic process of premature ovarian exhaustion. The earlier the menopause, the more severe and complex is the impact on sexuality.[3-5] The younger the woman, the less she realizes the different key goals of her life cycle (falling in love, having a satisfying sexual life, forming a stable couple, getting married, having a family) and the more pervasive the consequences on her sexual identity, sexual function, and sexual relationship can be.

Given the increasing number of women complaining of premature menopause, mainly as a result of prolonged survival after cancer treatment, the paper will focus on key sexual issues at menopause with this special perspective and a prominent attention on biologically based sexual issues, maintaining the key areas of sexual identity, sexual function, and sexual relationships,[1-15] while psychosocial variables will be only briefly addressed.[3] The goal is to empower

physicians' to better empathize about sexuality during the lifespan of a woman; once the attention is trained, confidence in dealing with this sensitive issue will increase for older women as well.

Women's wording of sexual concerns at menopause

To set the scenario, women's words are essential. They well describe the overall sense of sexual loss they feel when (early) menopause occurs. "Without my ovaries (or my uterus) I do not feel like a woman any more", and/or "Why should I make love, if I cannot have children anymore?" concisely explain why sexual identity, the sense of femininity and sexual attractiveness, as well as the potential for pregnancy are perceived as definitely wounded or lost .

"I do not have any sexual interest, for anybody, I feel sexually invisible" or "since I became menopausal, I have a worsening vaginal dryness; sex is no longer a pleasure. And now it hurts! That's why I came to consult you"; "I had an early menopause at 39. Now, at 45, it takes ages to get aroused, my orgasm is fading and weak. I'm too young to feel so old!" These quotes focus more on sexual function.

"We were looking for our first child. As the stork was not arriving, my gynaecologist requested hormonal samples: I'm getting menopausal! I'm distressed, but my husband is desperate. He has always longed for a child, and he said he cannot accept remaining childless. Please give me all the info on how I can get pregnant. Do I have a last chance with my ovary? Is ovum donation safe? I do not want to lose my husband. We feel so lonely and yet we cannot make love anymore...". This cry for complex sexual help indicates how pervasive the discovery of a premature menopause can be for the three dimensions of women sexuality, and how we must keep in mind the complexity, without limiting the listening and intervention to the sexual function. A multidisciplinary approach, both medical and psychosexual, may offer the most comprehensive and satisfying outcomes.

Premature menopause: a challenge for sexuality

The prolonged survival of children, adolescents, and young women successfully treated for cancer increases the number of women facing premature menopause (PM).[4,5] The complexity of their clinical picture, their increased vulnerability to accelerated aging for the combined effect of PM and side effects of chemotherapy and/or radiotherapy, their expectations for a better quality of life (QoL), both in general and sexual terms, challenge the physician' ability to tailor the more appropriate medical and psychosexual treatment.[4,5]

By definition, PM refers to menopause occurring at or before the age of 40. It may be spontaneous, and is referred to as premature ovarian failure (POF).[6-8] PM may be iatrogenic, i.e. secondary to surgical removal of both ovaries (bilateral oophorectomy), or to the irreversible ovarian damage caused by chemotherapy or radiotherapy, either pelvic or total body irradiation (Table 1).[4-8] The POF acronym currently encompasses all modalities of ovarian exhaustion, when the ovaries remain on site.

Surgical menopause *suddenly* deprives the woman of total ovarian hormone production, with a rapid impact on her wellbeing and sexuality**.** POF, either spontaneous or iatrogenic, has a gradual, *insidious* evolution over two or more years. Occasional ovulation is possible for 2-3 years after POF diagnosis.[7]

Given the trophic role of sexual hormones on body tissues, PM is associated with an increased risk of accelerated aging, the younger the woman, the higher the risk, unless appropriate hormonal treatment (HT), when feasible, is initiated and adequately maintained at appropriate doses.[2,3,5,9] Morbidity and mortality from cardiovascular disease, stroke, accelerated brain aging, and osteoporosis present a greater risk in PM women compared to controls. In particular, the recent research of Rocca et al. on the effect of mono or bilateral oophorectomy indicate an odds ratio of 1.46 of

accelerated brain aging in women who underwent this surgery in the fertile age; the younger the woman, the more vulnerable the brain.[9]

Sexual dysfunctions are reported with higher frequency and more significant personal distress after surgical menopause.[10] Overall sense of well-being and achievements of life goals are variably affected.

Prevalence of PM and associated FSD

Spontaneous POF affects on average 1% of women under 40 years of age.[7,9] Ethnicity is a contributor: the highest figure of POF is reported among African American and Hispanic (both 1,4%); the lowest in Japanese (0,1%).[16] Iatrogenic menopause, for benign and malignant conditions, affects 3.4-4.5% of women under 40.[2-5,17]

Systematic studies on prevalence of female sexual disorders (FSD) in women affected by PM are limited**.** The prevalence of low desire for younger surgically menopaused women is significantly higher (32%) than that found for premenopausal women of the same age (19%)**.** The probability of hypoactive sexual desire disorder (HSDD) increases with age, while the *distress* associated with the loss of desire is inversely correlated with age.[18]

Aetiology and diagnosis of PM and health vulnerabilities

Heterogeneity is the hallmark of the PM aetiology, which can be: genetic, autoimmune, associated with chronic diseases, or iatrogenic in the context of benign or malignant disease (Table 1). [3-9] PM impact on health and sexuality varies accordingly. It may be limited in women affected by POF, who have a family and are on optimal HT**.** It may be dramatic when the consequences of PM are superimposed to a serious medical condition which currently contraindicates HT, such as breast cancer, and/or in a childless younger woman and couple.[5,19,20] Multiple pathologies (and associated treatments) further increase the risk of accelerated aging, as exemplified when PM is associated to cancer or autoimmune diseases.

Impending PM is hypothesized when menopausal symptoms appear in women younger than 40 years of age, leading to POF. Predictors of PM include both poor response to ovarian stimulation and raised basal FSH. Definite diagnosis is based on FSH levels above 40 IU/L in two consecutive samples at one month distance.[7,9] Echography may show small ovaries for the age, with no or a few residual oocytes. PM is implicit when bilateral oophorectomy is performed in women younger than 40 years of age.

Factors modulating aging and sexual issues after PM

Aetiology of PM is the single most powerful biological factor affecting quality of aging and psychosexual outcome. Age at PM is critical; the earlier the PM occurs, the more complex the impact on general health and sexuality.[4,5]

Sexual identity is more vulnerable when PM disrupts the process of psychosexual maturity, after peripubertal spontaneous POF, or after iatrogenic POF, for childhood or adolescent cancers.[4,5] Stage in life cycle may contribute to FSD, fertility being a major issue in childless women and couples.[3-5,11]

Body image concerns, skin changes, changes in body shape and tendency for weight gain and central adiposity may impair the sense of personal attractiveness, contributing to loss of self-confidence and self-esteem, and a general sense of "feeling and looking older".[4,5,19-21] Dismetabolic diseases, diabetes first, are at higher risk in overweight PM women, and generally in obese menopausal subjects. Corticosteroids, when needed to treat the leading autoimmune pathology, such as lupus erithematosus systemicus (LES) or rheumatoid arthritis (RA), further increase this risk. Body image issues

may become prominent in women who underwent breast or gynecologic oncology surgery and associated treatments causing PM.[5,19-21]

The woman's health, coping attitude, and quality of sexuality *before* PM may all affect the sexual outcome after PM. Women at higher risk of negative sexual outcome after PM are younger, single or in conflicting relationships, childless, with lower education and socioeconomic status.[5,19-22]

The partner's reaction to the associated infertility and the quality of the relationships before and after PM further modulate the individual and couple's coping attitudes. Contextual factors – both relational and socio-cultural, such as ethnicity - further contribute.[11]

Pathophysiology of sexual dysfunction after PM

Oestrogens and androgens modulate the neurobiology of brain aging. Their trophic role in neuronal membrane repair, in promoting neuronal sprouting and interneuronal connectivity as well as the levels of neurotransmitters, is gaining increasing evidence. They also modulate sexual desire and mental arousal, and the neurovascular cascade of events leading to genital arousal, lubrication, and orgasm. Oestrogens are modulators of sexual response, and "permissive" factors for the vasoactive intestinal polypeptide (VIP), which "translates" desire and central arousal into vaginal congestion and lubrication.

Testosterone has an initiating role on desire and central arousal, acting on the dopaminergic appetitive-seeking pathway, and a modulator role of the peripheral response, as a permissive factor for nitric oxide (NO), the main mediator of clitoral and cavernosal bodies congestion.[4,5,23]

Loss of oestrogens and androgens contributes to impaired brain aging, as exemplified by increased and anticipated neurovegetative, affective, and cognitive disorders in PM women. It reduces sexual desire, central and peripheral arousal, with vaginal dryness, and causes/worsens orgasmic difficulties and dyspareunia, causing loss of self-confidence and self-esteem, and increases anxiety and concerns. Sexual hormone loss may as well contribute to the neurobiological aetiology of depressed mood that coexists so often with acquired loss of desire, and potentiates the depressive feelings consequent to the many losses that PM – and menopause in general - implies.[24]

Comorbidity of FSD is frequent. The issue of FSD cannot be separated from the impact on sexuality of concomitant medical comorbidities associated with or consequent to different aetiologies of PM.[5]

Diagnosis of FSD after PM

FSD may be antecedent to PM, concomitant to PM, and/or specifically caused and/or maintained by PM. Diagnosis should consider the multifactorial aetiology of FSD (with special attention to predisposing, precipitating and maintaining factors, biological and psychosexual), the disorder being generalized or situational, lifelong or acquired, as well as the level of distress it causes.

In stable relationships, counselling to *both* partners is a crucial part of the diagnosis and management. Accurate physical examination is mandatory, given the importance of biological disruptions associated to PM, with focus on trophism of external genitalia, vagina and vaginal pH, pelvic floor tonicity and "pain map", in case of dyspareunia.[5,25] A poor quality of genital sexual feed-backs is usually an under evaluated contributor of loss of sexual desire in PM and menopausal women.

Exams may include plasmatic hormone sample, when POF diagnosis has not yet been established, and vaginal pH. Specific exams should be considered according to the clinical history and aetiology of PM.

Treatment of PM and associated fertility issues

Tailored HT is the treatment of choice in POF, and in natural menopauses as well[2] (when non-contraindicated, i.e. in survivors of breast cancer or genital adenocarcinoma, or after thromboembolic disease, acute hepatitis etc.). Systemic oestrogen treatment (ET) is the choice in women who underwent hysterectomy besides oophorectomy. Topical vaginal ET may address vaginal atrophy and bladder symptoms when systemic ET is not suitable or desired.

Recommendations from the European Menopause and Andropause Society (EMAS) [26] and the International Society of Menopause (ISM) [27] include PM being HT treated, up until the age of natural menopause (51 years of age), unless a specific contraindication is diagnosed.

Prevention of infertility in women facing impending POF is critical in childless women. Three lines of *research* are currently raising new hopes in the pursuit of fertility protection in young women. Cryopreservation: a) of oocytes is an option in women with impending POF; b) of embryos is feasible, but requires a cycle of in vitro fertilization (IVF): time before cancer treatment may be a key limiting factor; [28] c) of ovarian tissue is promising.

Temporary ovarian suppression with goserelin may be an option for women with ER positive breast cancer. [29]

However, with an impending PM the current possibility of having a child is very rare. An honest disclosure of current limits of all these techniques should be clearly acknowledged in counselling with patients and their partner.

Management of general health and sexual issues associated to PM

The most important sexual issues are related to: 1) age, physical and psychological impact of PM or natural menopause; 2) effects of oestrogen and androgen loss on general and sexual health; 3) severity of menopausal symptoms; and 4) loss of fertility and its meaning to both partners.[5] An interdisciplinary approach offers the best opportunity to tailor treatment according to the woman and couple needs.

HT is the etiological treatment, when feasible, that may minimize the impact of PM on general health, menopausal symptoms and signs. The focus here will be on treatment of FSD associated to PM or natural menopause. An updated critical review of available treatment for menopausal FSD has recently been published by Al-Azzawi et al (2010).[2]

Medical management of FSD

Desire and central arousal disorders

Desire and central arousal overlap. Randomized controlled trials (RCT) indicate the positive effect of testosterone in oestrogen repleted women after surgical menopause, when aetiology of FSD appears to be hormone dependent. RCT have shown that treatment with 300-µg/d testosterone patches on oestrogen repleted women significantly increased sexual desire, frequency of satisfying sexual activity, reduced sexual distress, and was well tolerated.[12-15] Two systematic reviews of RCT indicate a positive effect of testosterone on all dimensions of sexual function and some psychological benefits as well.[24,30]

Secondary outcomes indicate a significant improvement of arousal and orgasm, of self-image and self-esteem, and a significant reduction in anxiety and concerns. The testosterone patch treatment has been approved by the European Agency for the Evaluation of Medicinal Products (EMEA) on July 2006. However, controversy still exists on the indication of androgen therapy in women.[31]

Tibolone and HT with estradiol and noretisterone are other options to improve sexual desire. Bupropion is a non-hormonal drug that may as well improve it.

Genital arousal disorders

Vaginal dryness, the leading complaint of genital arousal disorders, can be treated with vaginal estrogens.[32] Safety of vaginal oestrogen therapy has been documented in RCT and in observational studies such as the Million Women Study, which demonstrated that the relative risk of breast cancer was 0.67 no matter what type of vaginal oestrogen was used.
Vaginal estrogenic treatment is indicated when the genital arousal disorder causes and/or is associated with vaginal dryness, dyspareunia, post-coital cystitis, urogenital atrophy and/or urinary incontinence, mostly of the urge type.[5,25] Accelerated urogynecological comorbidity will be delayed with appropriate HT. Early vaginal estrogenic treatment, pelvic floor stretching and vaginal moulds, to maintain vaginal elasticity, optimal length and "habitability" during pelvic or vaginal radiotherapy for squamous cervical cancer, may minimize the impact of radiotherapy on vaginal tissue.
Testosterone cream (2% in vaseline jelly or petrolatum) applied in minimal quantity daily to the vulva may anecdotally improve vulvar trophism, clitoral sensitivity, genital arousal, and erotic response. It may therefore improve the genital feedbacks that may contribute to maintain sexual desire and central arousal. However, controlled studies are missing.

Orgasmic disorders

True orgasmic disorder acquired subsequent to PM may benefit from HT. Increasing evidence supports a positive role of testosterone in restoring orgasmic potential.[12-15, 24,30] Pelvic floor rehabilitation is indicated when hypotonia is diagnosed as contributing to reduced orgasmic sensations. Comorbid urge or stress incontinence with fear of leakage with orgasm is to be appropriately addressed.[5]

Sexual pain disorders, i.e. dyspareunia

Dyspareunia requires a careful pathophysiologic understanding of its complex biological aetiology (muscular, endocrine, vascular, nervous, immune, iatrogenic) and meaning, to design an effective treatment.[25] Friction introital dyspareunia, secondary to vaginal dryness, may benefit from vaginal ET. Reflexive pelvic muscle tightening ("hyperactivity of the elevator ani", secondary to pain) may benefit from self-massage and stretching, electromyographic biofeedback, and/or physiotherapy.

Psychosexual management

Psychosexual support to improve FSD includes individual behavioural therapy; psychotherapy to cope with the many losses PM and its aetiology have caused on health and sexuality; and couple therapy to address nonsexual couple issues, such as conflicts, poor erotic skills, or communication inadequacies. When the lack of an orgasm is associated with poor arousal, the latter is the first focus of psychosexual treatment.
In case of dyspareunia, psychosexual therapy includes behavioural therapy, vaginal inserts/moulds, progressive rehabilitation of the pelvic floor and, if necessary, pharmacological treatment for any intense phobic avoidance.

Couple issues after the menopause

In women with either POF or natural menopause, appropriate listening to the sexual concerns and to the real personal motivation to treatment is essential for treatment planning. After the natural menopause, 48% of women [10] report low desire, but only a minority feel distressed because of it and motivated to seek for treatment. Moreover, the older the woman, the higher the probability that the partner himself may have concomitant personal sexual problems, i.e. male sexual disorders (MSD), that may pre-exist to menopause, be concomitant to it, or consequent to the many FSD menopausal women may complain about.[3] The partner can be the "*symptom inducer*": when, for example, his persistent or worsening erectile deficit may cause or contribute to her loss of desire; or when his inadequate personal care or

hygiene precipitates her loss of sexual interest; or he can be the "*symptom carrier*", when his loss of desire is consequent to her avoidant behaviour towards any form of sexual intimacy; or when her vaginal atrophy, with dyspareunia and introital narrowing "precipitates" his erectile deficit, while erection could have been still acceptable, although not perfect, with a well lubricated vagina. The key message is to evaluate – and treat, when indicated - both partners, to have a comprehensive diagnosis of his/her contribution to the current sexual complaint.

Conclusions

PM accelerates general health and sexual aging, unless appropriate HT, when non-contraindicated, is initiated and maintained over time. FSD reporting after PM increases. Women with PM are at higher risk for distressing sexual disorders. RCT indicate that HT, with oestrogen and testosterone, may have positive effects on all domains of sexual function, especially after surgical PM.

Positive outcomes of RCT on 300 microgram testosterone patches in treating desire disorders (and associated FSD) in surgically menopausal women may offer more effective pharmacologic options for women complaining of FSD after PM. However, women and partners should be informed about the "lag time" (up to two, three months) between onset of treatment with testosterone patches and sexual improvement. This "waiting time" could be constructively used to address concomitant psychosexual issues (personal and/or partner related) and to (re)explore the sexual map after the difficult period of PM diagnosis.

More studies are needed to improve fertility protection in women undergoing POF, to evaluate long term safety of HT and its efficacy in reducing the accelerated aging associated with PM, and to assess the more effective treatment strategies to address women's (and couple's) sexual complaints after PM.

Attention to sexuality may be essential and welcomed as well for women after a natural menopause, in spite of the increasing difficulty older women have to raise sexual issues. The caring gynaecologist may ease the dialogue with a simple, open question: "How's your sexual life?", or with a more indirect statement: "Many women would like to maintain a satisfying sexual intimacy over the years, but the menopause may cause many sexual difficulties to them and/or to the couple. Is everything fine with you or is there any sexual concern you'd like to discuss?" Whatever the opening sentence, the more the woman feels that the gynaecologist is at ease with this issue, the more she will be willing to raise her concerns to get a proper diagnosis and treatment. In sexual medicine, as in every area of clinical work, "it's difficult to realize an effective intervention, if there is no mention of a problem". A well-tailored, integrated medical and psychosexual approach may offer women and couples a long lasting satisfying sexual season well after the years of an (early) menopause.

References

[1] Graziottin A. 1998. The biological basis of female sexuality. Int J Clin Pharm; 13 (Suppl 6): S15-S22

[2] Al-Azzawi F. Bitzer J. Brandenburg U. Castelo-Branco C. Graziottin A. Kenemans P. Lachowsky M. Mimoun S. Nappi R. Palacios S. Schwenkhagen A. Studd J. Wylie K. Zahradnik H-P. (FSD Education Team) 2010. Therapeutic options for postmenopausal female sexual dysfunction. Climacteric. 13 (2): 103-20

[3] Graziottin A, Leiblum SR. 2005. Biological and psychosocial pathophysiology of female sexual dysfunction during the menopausal transition. J Sex Med; 2 (Suppl 3): 133-145

[4] Madanat LMS, Malila N, Dyba T, Hakulinen T, Sankila R,. Boice JD, Jr, and Lähteenmäki PM. 2008. Probability of parenthood after early onset cancer: A population-based study. Int J Cancer. 123 (12): 2891-2898

[5] Graziottin A. Basson R. 2004. Sexual Dysfunctions in women with Premature Menopause. Menopause 11 (6): 766-777

[6] Fassnacht W, Mempel A, Strowitzki T, Vogt PH. 2006. Premature ovarian failure (POF) syndrome: towards the molecular clinical analysis of its genetic complexity. Curr Med Chem. 13 (12): 1397-410

[7] Meskhi A and Seif MW. 2006. Premature ovarian failure. Curr Opin Obstet Gynecol. 18 (4): 418-26

[8] Anasti JN. 2006. Premature ovarian failure: an update. Fertil. Steril 70: 1-15

[9] Rocca WA, Bower JH, Maraganore DM, Ahlskog JE, Grossardt BR, de Andrade M, Melton LJ 3rd. 2007. Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause. Neurology 69 (11): 1074-83

[10] Graziottin A. Koochaki P.E. Rodenberg C. Dennerstein L. 2009. The prevalence of hypoactive sexual desire disorder in surgically menopausal women: an epidemiological study of women in four European Countries. J Sex Med, 6 (8): 2143-2153

[11] Rauck A, Green DM, Yasui Y, Mertens A, Robinson LL. 1999. Marriage in the survivors of childhood cancer: a preliminary study description from the Childhood Cancer Survivor Study Medical and Pediatric. Oncology 33: 60-63

[12] Shifren JL, Braunstein J. Simon JA, et Al. 2000. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. New Engl J Med 343: 682-688

[13] Buster JE, Kingsberg SA, Aguirre O, et Al. 2005. Testosterone patch for low sexual desire in surgically menopausal women: a randomized trial. Obstet Gynecol. 105 (5 Pt 1): 944-52

[14] Simon J, Braunstein G, Nachtigall L, et Al. 2005. Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. J Clin Endocrinol Metab. 90 (9): 5226-33

[15] Davis SR, van der Mooren MJ, van Lunsen RH, et Al. 2006. Efficacy and safety of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. Menopause. 13 (3): 387-96

[16] Luborsky, JL, Meyer,P, Sowers, MF, Gold, EB, Santoro, N. 2003. Premature menopause in a multiethnic population study of the menopause transition. Hum Reprod 8 (1): 199-206

[17] Puukko LMR, Hirvonen E, Aalberg V, Hovi L, Rautonen J, Siimes Ma. 1997. Sexuality in young women surviving leukemia. Arch disease childhood 76: 197-202

[18] Graziottin A. 2007. Prevalence and evaluation of sexual health problems – HSDD in Europe. J Sex Med 4 (suppl. 3); 211-219

[19] Schover LR. 1994. Sexuality and body image in younger women with breast cancer. J Natl Cancer Inst Monogr. 16: 177-82

[20] Graziottin A, Castoldi E. 2000 Sexuality and breast cancer: a review. In: Studd J, ed. The management of the menopause. The millennium review 2000, London, UK: Parthenon Publishing, 211-220

[21] Graziottin A. 2006. Breast cancer and its effects on women's self-image and sexual function.

In: Goldstein I. Meston C. Davis S. Traish A. (Eds), Women's Sexual Function and Dysfunction: Study, Diagnosis and Treatment, London, UK: Taylor and Francis, 276-281

[22] Graziottin A. 2005. The woman, patient after WHI. Maturitas, 51 (1): 29-37

[23] Bachmann G, Bancroft J, Braunstein G, et Al. 2002. FAI: the Princeton consensus statement on definition, classification and assessment. Fertil Steril 77: 660-665

[24] Alexander JL, Dennerstein L. Burger H, Graziottin A. 2006. Testosterone and libido in surgically and naturally menopausal women. Womens' Health 2(3): 459-477

[25] Graziottin A. 2006. Sexual pain disorders (Dyspareunia and vaginismus). In: Porst H & Buvat J (Eds), ISSM (International Society of Sexual Medicine) Standard Committee Book, Standard practice in Sexual medicine, Oxford, UK: Blackwell, 342-350

[26] Skouby SO and the EMAS (European Menopause and Andropause Society) Writing Group 2004. Position statements on postmenopausal hormonal therapy. Maturitas 48: 19-25

[27] Burger H. and the IMS (International Menopause Society) Writing Group 2004. Practical recommendations for hormone replacement therapy in the peri and post menopause. Climacteric 7: 1-7

[28] Oktay K, Buyuk E, Davis O, Yermakova I, Veeck L, Rosenwaks Z 2003. Fertility preservation in breast cancer patients: in vitro fertilization and embryo cryopreservation after ovarian stimulation with tamoxifen. Human Reprod. 18: 90-95

[29] Jonat W, Kaufmann M, Sauerbrei W, et Al. 2003. Goserelin vs. cyclophospamide, methotrexate, and fluorouracil as adjuvant therapy in premenopausal patients with node-positive breast cancer: the Zoladex Early Breast Cancer Research Association Study. J Clin Oncol. 20 (24): 4628-4635

[30] Somboonporn W, Davis S, Seif M, Bell R, Davis S 2005. Testosterone for peri and postmenopausal women. Cochrane Database Syst Rev: CD004509

[31] Wierman ME, Basson R, Davis SR, Khosla S, Miller KK, Rosner W, Santoro N 2006. Androgen therapy in women: an endocrine society clinical practice guideline. J.Clin Endocrinol Metab. 91 (10): 3697-710

[32] Goldstein I. Alexander JL. 2005. Practical aspects in the management of vaginal atrophy and sexual dysfunction in perimenopausal and postmenopausal women. Review. J Sex Med. 2 (S.3): 154-65

Table 1. Aetiology of premature menopause

Premature Ovarian Failure (POF):

- idiopathic
- genetic:
    - Turner's syndrome
    - fragile X syndrome
    - mosaicism
    - deletion/inversion
    - galactosaemia
    - BRCA1 mutation
- autoimmune:
    - lupus erythematosus
    - rheumatoid arthritis

- associated with chronic disease:
    - chronic renal insufficiency
    - primary biliary cirrhosis

Iatrogenic for benign conditions:

- endometriosis
- bilateral disgerminoma
- ovariectomy concomitant to hysterectomy

Iatrogenic in women at risk of ovarian cancer:

- BRCA1 and/or BRCA2 carrier

Iatrogenic for established malignant conditions:

- bilateral oophorectomy
- chemotherapy
- pelvic radiotherapy
- total body irradiation

Modified from Graziottin & Basson, 2004 [5]