DESIRE DISORDERS:
ENDOCRINOLOGICAL ETIOLOGIES
& TREATMENT PERSPECTIVES

Dr Michèle BUVAT-HERBAUT
97 avenue Marx Dormoy
59000 LILLE (France)
HYPOACTIVE SEXUAL DESIRE IN WOMEN

• Until 6 years ago, the definition of sexual disorders was focalized upon psychological and/or relational components of one woman in her couple, and was detailed in the Manual of Psychiatric Disorders (the last was The Fourth Edition, DSM 2000).

• Recently, there has been a resurgence of scientific interest. Researchers and clinicians (coming from very different specialties and countries) have worked together to develop definitions of female sexual dysfunction based on the different domains of female sexual functioning (desire-arousal-orgasm) and sexual pain.
HYPOACTIVE SEXUAL DESIRE IN WOMEN

• Since the Second International Consultation on Sexual Medicine which stood in Paris, in 2004, experts decided refining the definition and proposing the validation of new tools to measure the different aspects of female sexuality and associated distress.

• The Hypoactive sexual desire is defined as the persistent or recurrent deficiency of sexual fantasies / thoughts and / or desire for sexual activity, that causes personal distress.

• This sexual dysfunction is apart from arousal, orgasm & pain disorders.
HYPO ACTIVE SEXUAL DESIRE IN WOMEN

- On a methodological level, advances have also been done in proposing well-studied questionnaires, including one depression scale.
- These questionnaires are:
  - 1) The Life Satisfaction Check List: 9 questions with 6 possible answers (Life in general; relational problems/partner; friends; leisure; work problems...)
  - 2) The Medical History Questionnaire (MHQ): 7 questions with 4 or 7 possible answers (in which the average frequency of sexual activity, and the age when this problem appeared).
  - 3) The Supplemental Questions Regarding sexual Health: 4 questions: 1) average frequency of intercourses/week or month
    - 2) the orgasm frequency
    - 3) starting event or not
    - 4) vaginal dryness (score 0 to 7)
HYPO ACTIVE SEXUAL DESIRE IN WOMEN

• Other questionnaires are available:


• 5) The Female Sexual Distress Scale (FSDS): a woman is considered as dysfunctional only if her score is more or equal 15 (and 3 items > 3).

• 6) The Sexual Quality of Life Questionnaire-Female (SQoL-F).

• The answers to these questionnaires will lead to the diagnosis of an Hypo Sexual Desire Disorder, which causes a personal distress.
HYPO ACTIVE SEXUAL DESIRE IN WOMEN

• Before to speak about the prevalence of this disorder, we must insist on the fact one woman is unique.

• The age range is very important: the sexuality of a young woman has not yet penalized by the co-morbidity of pathologies related to age, or by the couple-conflicts. The type or the absence of contraception must be precised. The girls who start their sexual life will feel insecure or ashamed if the principle of a contraception is not allowed because of cultural & religious restrictions.

• Later: 1) The consequences of pregnancies upon the uro-genital tract must be evaluated. 2) Has she been operated? Which surgery? Are there co-morbidities? (for instance, as regards urologists: ask about pelvic floor disorders, incontinence, uro-genital prolapse...).

• Urologists must not forget that a cancer history (even extragenital) may have negative effects / sexuality through psychological angles (a woman may badly accept her body spoiled by surgery).
HYPOACTIVE SEXUAL DESIRE IN WOMEN

• 3) Is there a chronic disease as diabetes, or thyroïd disfunction ?
• 4) Is there another chronic disease ( as cardio-vascular, neurological, or psychiatric problems ) ?
• 5) Is there a pharmacological treatment which may interfere with sex steroïds or neuro-transmitters ?
• 6) Is there substance abuse ?
• 7) Is there an hyperprolactinaemia ( an high prolactin inhibits sexuality ) ?
• 8) Is there a chronic hypoestrogenism related to anorexia nervosa; but also patients treated by GnRH-agonists : ex : endometriosis.
• 9) Is there an history of Sexually Transmitted Disease ?
• 10) A bad weight control is bad for body-image and mood.
• 11) A little sleep may evoque a subdepressive state. ( depression decreases sexual desire ).

IN POST-MENOPAUSAL WOMEN : has menopause been natural or surgical ? One Hormone Replacement Therapy ( HRT ) has been prescribed ? For how long ? Did it improve sexual life ?
HYPOACTIVE SEXUAL DESIRE: PREVALENCE

- In France, in 2003, a study about prevalence of sexual dysfunctions has been realized in 1002 subjects (in which 519 women, aged > 35 years) by Marie-Hélène Colson (& Lilly Laboratories) and published in the Journal of Sexual Medicine (2006; 3: 121-131). 46% of the women report a decrease of sexual desire.
- In Western Europe: a cross-sectional survey realized by Lorraine Dennerstein & Alessandra Grazziotin has been published in another Journal of Sexual Medicine (2006; 3: 212–222). 2467 women have been questioned (aged: 20 – 70 years) by means of « new generation » questionnaires and using a distress scale.
- The Hypoactive Sexual Desire (DSH) is the most frequent dysfunction (with sexual distress).
  - age range: -20-49 years: 7% DSH in premenopausal women and 16% DSH after surgical menopause
  - 50-70 years: 9% DSH when natural menopause and 12% DSH after surgical menopause

These percentages show that female sexual function declines with age (and with menopause). But women report less distress with age.
HYPO ACTIVE SEXUAL DESIRE

ALWAYS, TO REMIND THAT EACH WOMAN HAS HER OWN PSYCHOSEXUAL PECULIARITIES:

- her age: +++
- her sexuality results: - from the dynamism of the couple
  - from the personal, educational, professional & relational cursus
  - from the cultural & religious back-ground
  - by after-effects of her medical or surgical history

Lastly, the sexual dysfunction is reinforced by well-known vicious circles (for instance, at the occasion of a psychological traumatism: death of a child, divorce…).
HYPO ACTIVE SEXUAL DESIRE

• **Biological descriptors** will be decided according to each personal history: research of metabolic disorders (as diabetes, and casually thyroïd dysfunction). (serum TSH assay).

• A serum-prolactin assay may be indicated (if an hyper-prolactinaemia is confirmed, specific radiological exams will be decided, and specific dopaminergic agonist drugs will be prescribed).

• The assay of plasmatic FSH (Follicle Stimulating Hormone) (which reflects the age of the ovaries): its interpretation is much debatable in women aged more than 35 years.

• The assay of sex steroïd hormones (as estrogens or androgens) concerns the research field, and not the clinical practice.
HYPO ACTIVE SEXUAL DESIRE : TREATMENT

• IN YOUNG WOMEN : a medical approach may have a positive effect upon the future sexual life.
  • That means to explain the interest of a contraception.
  • That means sexual counselling ( better intimacy; to find better conditions for the first intercourses…).

• IN POST-MENOPAUSE : for many years, one Hormone Replacement Therapy ( HRT ), using estrogens + or not progestins, has been proposed to these women, in order to replace the estrogen-cessation by the ovaries.
  • HRT short-term effects were to stop hot-flushes, and to impeed vaginal dryness which does not allow a satisfying sexuality.
  • HRT long-term effects were supposed to be protective at the cardio-vascular level; against cognitive troubles, and mainly was efficacious against post-menopausal bone loss. So, HRT allowed the women aging in better conditions with less osteoporotic fractures.
HYPO ACTIVE SEXUAL DESIRE : TREATMENT

• IN POST-MENOPAUSE :

• For many years also, a post-menopausal woman, by her hypo-gonadism, has constituted one ideal experimental subject, in order to evaluate the effects of HRT.

• The HRT cessation will also have perverse consequences : indeed, it is likely that we will have less drugs available in the sexually dysfunctional women.

• And that it is paradoxal, when we understand that a longer duration of life in general, will mean a longer duration of life in post-menopause.
WHY THIS HRT CESSION ?

• In 2002, the publication of the US study WHI (Women Health Initiative) has provoked a revolution.
• Then in 2003, the english « Million Women Study », then in France, the study E3N would show a slight increase of breast cancer in the HRT group, compared to the placebo group.

Another point: the protective effect of HRT upon cognitive troubles has not been confirmed.

The french study (ESTHER), about the thrombo-embolism risk, has shown this risk was not increased if percutaneous estrogens were used. Indeed, the US and english studies have shown an increase risk of thrombo-embolism and ischemic events.

It was difficult to compare the results of the US studies to the french ones: in France percutaneous estrogens have been used for many years, associated to very different progestins (in US, the usual HRT was PREMARIN = conjugated equine estrogen + medroxy-progesterone acetate). The profile of the US patients was also different (higher age & weight).

Nevertheless, the positive point of the WHI study has been to confirm the protective effect upon bone loss in the women under HRT, compared to the non-treated groups.
APART HRT, WHICH DRUGS ARE AVAILABLE IN POST-MENOPAUSE?

- **SERM**: (Selective Estrogen Receptor Modulator)

  * **Raloxifene** (EVISTA, OPTRUMA): its efficacy has been confirmed upon post-menopausal bone loss, without effect neither upon cardio-vascular function, nor on breast. It exerts no negative or positive effect / sexuality.

  * **Tibolone** (LIVIAL): its efficacy upon hot-flushes is not so good as a classical HRT, but better upon sexuality. The «Liberate Study» (which evaluates tibolone / HRT in women having an history of breast cancer) will be published in 2008. Rosemary Basson has reported in 2003 the conclusions of a panel of north-american experts: it would decrease the risk of vertebral fracture, and increase this of ischemic events.

  * **Lasofoxifene**: has shown an improved dyspareunia in case of vaginal dryness. We don’t know this SERM’s effects upon sexual dysfunctions in post-menopause.
HYPOACTIVE SEXUAL DESIRE AT ANY AGE

- phosphodiesterase type 5 inhibitors: as in males, in vitro studies have shown the presence and distribution of PDE5 in the human vagina, which suggest the integrated system of nitric oxide (NO) synthase. PDE5 may play a physiological role in female sexual arousal.

The efficacy of sildenafil citrate (VIAGRA) which has been the first PDE5 inhibitor evaluated in clinical trials, in very different female patient cohorts. Unluckily, in spite of a big hope waited at the beginning, the superiority of sildenafil/placebo has been proved in hyper–selected cohorts of female patients: for instance, in a cohort of 202 post-menopausal women presenting sexual arousal disorders without associated HSD (Jr & La Berman in 2003) (treatment duration = 12 weeks).

Similar results have been reported in other types of hyper-selected women: ex: a multiple sclerosis (Das Gupta et al, J Urology 2004, 171: 1189 – 1193); or women with spinal cord injury (Sipski et al, Urology 2002, 55: 812 – 815); or in psychotropic-induced sexual dysfunction (Salerian, 2000).

Other PDE5 inhibitors as tadalafil (CIALIS), or vardenafil have shown better results/sildenafil.

I. Goldstein et al have recently reported that restoring the erectile function of the partner allows to improve the sexual life of the spouse.
HSD : OTHER DRUGS AVAILABLE?

- **Apomorphine**: (as in males) has been proposed. It may be efficacious if high concentrations are used, with serious side-effects.
- **Yohimbine + arginine**: unclear conclusions.
- **Alprostadil**: (as in males) has been proposed (clitoral maasages). Results to be confirmed (Gittelman 2005).
- The local use of lubricating non hormonal or hormonal jellies may be proposed (in which estriol preparations).
- Androgens’ adjunction: the impact of androgens upon the female sexual function is badly known. Nevertheless, there is a consensus that this adjunction has a positive effect upon sexual drive and well-being in general. It is likely this adjunction allows the obtention of a supra physiological estrogen concentration (after aromatization of androgens) at the central level.
- Products are available in many ways of administration: nasal spray-pellets-oral androgens (PANTESTONE) – percutaneous gel (local use) or transdermic patches.
- Androgenic precursors, as DHEA, have also been proposed (ISSWH, 2005 A Guay).
RISKS OF THE USE OF ANDROGENS

- We must appreciate the risks of this androgens’ adjunction:

  * short-term: slight side-effects (as acne or hirsutism)
    - the risks of foetal virilization in utero in case of women still in age of procreating.

  * long-term:
    - the risk of modifying the blood lipid profile, and coagulation activation
    - an increased risk of breast cancer is not excluded: a recent prospective cohort-study, published by Tamini (Nurses’ Health Study): long duration study (x 24 years), including > 1.300.000 subjects / year. The Relative Risk (RR) of breast cancer attains 2.48 in the group of women whose HRT associated estrogens + testosterone.
HRT CESSATION: CONSEQUENCES

• 1° Most of the patients stopped their HRT. Some women prefer using phytoestrogens, though their potential effects have not been controlled.

• 2° To have to consult regularly their gynaecologist (in order to get the HRT prescription) allowed a better diagnosis of breast cancer (or of other gynaecologic cancers) by means of the clinical examination and prescription of mammograms.

• 3° The other long-term consequence will be to take care of osteoporosis by other means which must be debated.
CONCLUSIONS

- Advances had been recently performed in many fields of female sexuality

- Better definitions; better methodologies for future clinical trials; better quality of the questionnaires used for evaluating the medical history and the type of the sexual dysfunction.

- Unluckily, the HRT cessation will have perverse consequences and finally we will still have less drugs to propose.