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Sexuality

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Aging; Estrogen; Hormones; Menopause; Sexuality; Testosterone This article reviews changes in sexual function in middle-aged women and discusses how these changes relate to aging, hormone alterations, and psychosocial and physical factors. A Medline search of population-based studies that measured sexual function, menopausal status and/or hormone levels was conducted. Longitudinal findings are from the Melbourne Women's Midlife Health Project, a population-based sample of 438 Australian-born white women, aged 45 to 55 years, who were menstruating at baseline. Annual assessments included hormone levels and the Short Personal Experiences Questionnaire. Few of the population-based studies of the menopausal transition measured sexual function or hormones. Aging and the length of the woman's relationship with her partner are associated with decline in sexual function. An additional decrement in sexual function occurs in midlife associated with menopause. Findings from the Melbourne Women's Midlife Health Project using structural equation modeling, found the most important factors influencing a woman's sexual function are prior level of sexual function; losing or gaining a sexual partner; feelings toward a partner; and estradiol level. When psychosocial and lifestyle status were added to the model, mood was the only additional variable affecting sexual function. There is a decline in all aspects of female sexual function with age. A further incremental decline in most aspects of sexual function occurs as women pass through the menopausal transition and is related to decreasing estradiol levels. Other factors such as prior sexual function and partner issues have larger effects on women's sexual function than do hormonal factors. © 2005 Elsevier Inc. All rights reserved.

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The 3 critical physiologic requirements for female sexual function are as follows: intact sex steroids, autonomic/somatic nerves, and arterial inflow/perfusion pressure to the genital organs.¹ Sex steroids are known to play a crucial role in maintaining the anatomical and functional integrity of all structures involved in female sexual function.¹ Epidemiologic and double-blind clinical trials have focused on the role of estrogens (alone or in combination with progestins) and the androgen testosterone.^{1–3} Recent expert review¹ concludes that further studies are needed to clarify the relevance of sex steroids to women's sexual function.

This article reviews the changes that occur in the different domains of women's sexual function in middle age, and evaluates how these relate to the overall aging process, to hormonal changes of the menopausal transition, and to other psychosocial and physical factors. Clinicians have long been concerned about effects of menopause on female sexual function as sexual complaints are among the most frequently reported health concerns of women attending menopause clinics.⁴ Yet clinical experience is based on a small proportion of self-selecting women and may not be representative of most women's experience of the menopausal transition.⁵

There are a number of other possible explanations for deteriorating sexual function in this phase of life. Major confounders include the length of the woman's relationship with her partner, chronologic aging, other physical health problems, loss of her partner, the partner's health and medication usage, and the many psychosocial stressors associated with midlife.

Population-based studies provide information on the prevalence and type of changes in sexual function and their relation to menopausal hormonal changes and other possible determinants. These studies complement clinical trials that provide evidence on hormonal effects on specific parameters of sexual function in the groups studied.

Sexual function versus sexual dysfunction

Current definitions of female sexual dysfunction include both low sexual function and personal distress components for each of the domains of desire, arousal, orgasm, and pain.⁶ Studies published before the development of these definitions usually do not include measures of personal distress. Only a proportion of those who have low sexual function will be distressed about it⁷ and, hence, will be dysfunctional.

A number of studies concur in finding that women more frequently report low sexual desire or interest than do men and that there is poor correlation of women's subjective sexual arousal with observable increases in genital congestion in response to sexual stimulation.⁸ To address these findings, an expert panel convened by Basson and colleagues⁸ has reconceptualized women's sexual response. They found a circular model of overlapping phases of variable order influenced by psychological, societal, and biologic factors.

Methodologic limitations

Population-based studies enable the study of women in their own naturalistic setting. These investigations also assess the effects of factors other than hormonal changes. The results are then generalizable to the ethnic group and location studied. Most population-based studies of female sexual function have failed to include validated measures of female sexual function.² Measures used have mostly been single questions that addressed particular domains of function or that asked respondents to report their sexual problems or difficulties. Studies of large sample sizes often ask fewer questions with less assurance of a reliable answer than do smaller studies, which may be able to collect more detailed data. Based on our own experience of longitudinal studies of changes in health outcomes with the menopausal transition,⁹ a minimum baseline study population of 400 subjects is needed to provide enough power to detect change.

The age of subjects at baseline should be young enough so that measures are obtained before major change occurs in the hypothalamic-pituitary-ovarian axis. Documentation is needed of any use of hormone therapy (HT) and of surgery that may compromise ovarian function, such as hysterectomy. Also crucial to the inferences that can be drawn are the type of study (cross-sectional versus longitudinal), and statistical techniques that can unravel the complex interrelationships between outcomes and determinants.

Relatively few of the population studies of the menopausal transition in middle-aged women have inquired about sexual function. Even fewer have used a validated questionnaire to assess the different aspects of sexual function. A major problem has been to disentangle the effects of aging from that of menopause. The hormonal changes of the menopause take place over a variable period of time known as the menopausal transition, so that aging and menopause are inevitably confounded. Most epidemiologic studies have not directly measured hormonal status of the women surveyed, instead using menstrual status as a proxy for hormonal status.

Cross-sectional studies allow us to identify differences across age ranges, reproductive status groups, and ethnic groups. A major advantage of longitudinal studies is that of less reliance on retrospective data, providing that the recall period inquired about is kept short. Longitudinal studies of samples derived from the general population are in the best position to sort out whether there is a change in sexual function associated with the menopausal transition and, if so, whether this reflects aging, health status, or hormonal or psychosocial factors. A major advantage of longitudinal studies is the ability to control for the effect of prior level of sexual function.

For longitudinal studies, the length of prospective follow-up is crucial. For example, after 9 years of follow-up of our population-based Melbourne Women's Midlife Health Project cohort of women aged 45 to 55 years (mean age, 48 years) at baseline, 8% were still menstruating and 51% of the women had reached documented final menstrual period (FMP) without medical intervention. A total of 21% had begun HT before reaching their FMP, and 8% of the cohort had undergone surgical menopause.¹⁰

Effects of aging

Aging and length of the relationship with a partner are known to affect sexual function of both men and women,^{11,12} and these variables are often confounded. The longitudinal Melbourne Women's Midlife Health Project found a highly significant negative effect of aging on frequency of sexual activity; sexual interest (libido); and aspects of sex-

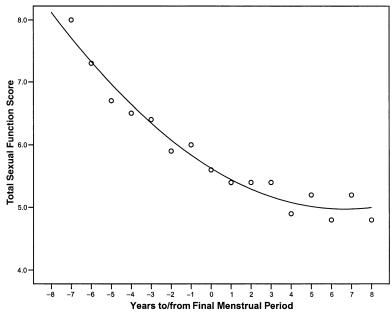


Figure 1 Total score of sexual function in relation to final menstrual period.

ual responsiveness, sexual arousal, enjoyment, and orgasm.¹³ In the Women's International Study of Health and Sexuality (WISHeS), a multinational cross-sectional study carried out concurrently in Europe and the United States using validated measures of sexual function and sexual distress, a decline in all aspects of sexual function was evident with age.¹⁴ Sexually related distress, however, decreased with age so that there was no increase in sexual dysfunction with age.¹⁴

Aging versus menopausal status

A number of studies have found an additional decrement in aspects of sexual function in midlife,^{15,16} coinciding with mean age of menopause¹⁷ or menopausal status where measured.^{18,19} Studies that failed to find effects of menopausal status have been limited by small sample sizes,¹² wide age ranges, and lack of validated measures.²⁰

Very few studies have followed the same cohort prospectively across the menopausal transition. Longitudinal studies allow us to disentangle the effects of aging from those of menopausal hormonal changes (which are inevitably confounded) as well as to measure the powerful effects of psychosocial factors, including the individual's own prior level of sexual function and changes occurring in sexual partnerships.²¹ The Melbourne Women's Midlife Health Project is a population-based sample of 438 Australian-born women who were aged 45 to 55 years at baseline and were still menstruating. The women have been followed with annual assessments and hormone measures for 13 years. The Personal Experiences Questionnaire short form (SPEQ), a validated measure of sexual function based on the McCoy Female Sexuality Questionnaire,^{22–25} was used. The

SPEQ scale provides domain scores for frequency of sexual thoughts (libido), arousal, enjoyment and orgasm (sexual responsivity), frequency of sexual activities, and dyspareunia. Feelings about partner and partner problems are also measured. A total score of sexual function is calculated from the domains of libido, sexual responsivity, and frequency of sexual activities. Scores ≤ 7 indicate low sexual function, similar to women with sexual dysfunction.²⁵ From early to late menopausal transition, the percentage of women with SPEQ scores of low sexual function increased from 42% to 88%.¹³ By the postmenopausal phase, there were significant declines in sexual responsivity, frequency of sexual activities, libido, and the total score of sexual function, combined with significant increases in dyspareunia and partner's problems in sexual performance.²⁶ Increasing dyspareunia and decreasing libido and responsivity correlated with decreasing estradiol but not with androgens.¹³ Figure 1 shows the decline in the total score of sexual function in relation to time to FMP.

Relative importance of hormonal and psychosocial factors

These results assist us in understanding the impact of the menopausal transition on women's sexuality. However, analytic techniques that can include psychosocial factors and the effects of increasing age are necessary to understand the relative importance of hormonal factors. Using techniques of autocorrelation and cross-correlation together with structural equation modeling, the Melbourne Women's Midlife Health Project found that for the 336 women for whom data were available for 8 years of follow-up, the most important factors (in decreasing order of importance) influencing do-

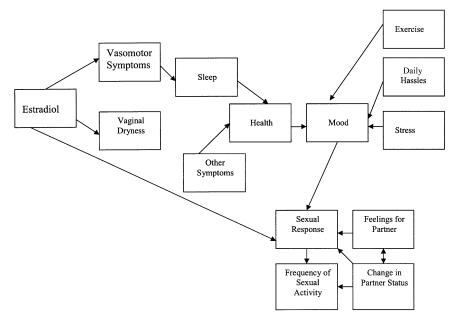


Figure 2 Longitudinal structural equation modeling of factors affecting sexual response.

mains of libido and sexual responsiveness (together termed sexual response) are prior level of sexual function, losing or gaining a sexual partner, feelings toward the partner, and estradiol level²⁷ (coefficient of determination for multivariate analysis $[R^2] = 0.65$). Relationship factors were less important for dyspareunia, which was predicted by prior level of dyspareunia and estradiol level ($R^2 = 0.53$). Frequency of sexual activities was not influenced by estradiol level but was predicted by prior level of sexual function, change in partner status, feelings for partner and level of sexual response ($R^2 = 0.52$). The minimum effective dose needed to increase sexual response by 10% (700 pmol/L estradiol) is twice that needed to decrease dyspareunia.²⁷ Endogenous testosterone (determined as the free testosterone index) and dehydroepiandrosterone sulfate were not related to sexual function domains.^{13,27} When a validated measure of distress (the Female Sexual Distress Scale) was included in the 11th year of follow-up, we found that only 17% of the women (then aged 57 to 67 years) were significantly distressed.7

The Melbourne Women's Midlife Health Project included measures of many variables found to influence domains of sexual function in cross-sectional studies. These include availability of a partner, well-being, educational level, parity, stress, mood, health status.²⁸ The study used longitudinal structural equation modeling to determine the most important influences on sexual response and frequency of sexual activity. Included in the modeling were potential determinants measured at baseline (education; parity; attitudes; premenstrual complaints) or annually over the course of 8 years of follow-up (hormone levels; partner's problems with sexual performance; change in partner status; feelings toward partner; stress; daily hassles; lifestyle factors; wellbeing; and self-rated health and bothersome symptoms, which were grouped into vasomotor, insomnia, other, vaginal dryness). The only additional factor found to affect the sexual function domains was well-being, as measured by the Affectometer 2 scale.²⁹ Well-being was itself affected by lifestyle factors, stress, daily hassles, vasomotor symptoms, sleep, and self-rated health (**Figure 2**).

Ethnicity

The Melbourne sample included only white Australian women. It is not clear whether there will be any ethnic variation in response to declining estradiol at menopause. Using cross-sectional data from baseline (when women had not begun the menopause or were early in the menopausal transition), the US-based Study of Women's Health Across the Nation (SWAN)²⁸ reported substantial ethnic differences in sexual domains. After controlling for a wide range of variables, African American women reported a higher frequency of sexual intercourse than white women; Hispanic women reported lower physical pleasure and arousal; Chinese and Japanese women reported more pain and less desire and arousal than the white women, although the only significant difference was for arousal.²⁸ Other studies carried out in Europe also have reported substantial differences between countries in domains of sexual function, such as frequency of sexual intercourse; but nevertheless they found a similar pattern of decline in the effects of menopause on desire, arousal, and orgasm across all countries.³⁰

Surgical menopause

This article has focused on changes related to the natural menopausal transition. Surgical menopause, in which both ovaries are removed, was predicted to have more deleterious effects on sexual function because all ovarian estrogen and androgen is removed.

Summary

There is a decline in all aspects of female sexual function with age. A further incremental decline in most aspects of sexual function occurs as women pass through the menopausal transition. This further decline is related to decreasing estradiol levels. Other factors such as prior sexual function and partner-related factors have larger effects on women's sexual function than do hormonal factors. However, when relationship factors are stable, declining estradiol has noticeable effects. Not all women with low sexual function are distressed about it.⁷

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