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A pioneer in menopause research, Dr. Utian founded the world's first menopause clinic in Cape Town, South Africa, in 1966 and established the Cleveland Menopause Clinic in 1983.

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The True Symptoms Associated with Menopause Confirmed after 33 Years: Better Late than Never, But Let's Move on Now!

It is quite extraordinary how frequently in medicine a finding published three, four, or more decades ago languishes in obscurity until, voila!—the observation is rediscovered and that idea then becomes the newly accepted dogma. This phenomenon was driven home to me with the publication of the summary statement from the March 21-23, 2005, National Institutes of Health (NIH) State-of-the-Science Conference, entitled "Management of Menopause-Related Symptoms."¹

In 1972, I published a paper based on several years of work on my doctoral thesis, entitled "The True Clinical Features of Postmenopause and Oophorectomy, and Their Response to Oestrogen Therapy."² The summary of my thesis reads, in part, as follows:

"The true clinical effects of endogenous oestrogen withdrawal following bilateral oophorectomy and menopause were assessed....The subsequent response of these effects to exogenous oestrogen therapy was determined, and true hormonal effects differentiated from simple placebo responses. It was found that the only symptoms directly associated with the menopause and occurring specifically after oophorectomy are those related to hot flushes and atrophic vaginitis. In turn, these symptoms are the only ones to be specifically relieved by exogenous oestrogen therapy...The symptoms of depression, irritability, angina pectoris, insomnia, and palpitations responded significantly to placebo therapy and are, therefore, most likely of psychological origin...the use of indiscriminate oestrogen therapy as a panacea against any 'postmenopausal symptom' other than hot flushes or atrophic vaginitis is condemned."

These findings formed the basis of a 1976 report compiled by an international task force, chaired by the late David Serr and me, convened at the First International Congress on Menopause in France to classify the symptomatology associated with menopause. The published summary statement reads as follows:

"Climacteric symptoms and complaints are derived from 3 main components:

- 1. Decreased ovarian activity with subsequent hormonal deficiency resulting in early symptoms (hot flushes, perspiration, and atrophic vaginitis) and late symptoms related to the metabolic change in the end organ affected.*
- 2. Sociocultural factors determined by the woman's environment.*
- 3. Psychological factors, dependent on the structure of the woman's character."*

Twenty-eight years later, these findings were confirmed in Melbourne, Australia. Based on data from a longitudinal, prospective, population-based study of menopausal symptoms in 438 women observed for 7 years, during which time 172 women advanced from premenopause to perimenopause or postmenopause, Dennerstein et al concluded: "Although middle-aged women are highly symptomatic, the symptoms that appear to be specifically related to hormone changes of the menopausal transition are vasomotor

symptoms, vaginal dryness, and breast tenderness. Insomnia reflected bothersome hot flashes and psychosocial factors.”⁴

The summary statement of the recent NIH meeting¹—which took place 33 years after my original report was written—confirmed that there is strong evidence that menopause causes vasomotor symptoms and vaginal dryness, moderate evidence that menopause is the cause of sleep disturbance in some women, and an absence of evidence showing that menopause might be a cause of depression, anxiety, and/or irritability. It also stated that there is insufficient information to conclude any causal relationship between the menopausal transition and difficulty thinking, forgetfulness, or other cognitive disturbances. Other than a definite relationship between painful intercourse and vaginal atrophy and dryness, a causal relationship between menopause and libido was considered not to have been established.¹

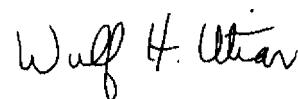
Clearly then, despite the fact that these reports come from four continents and vary vastly in dates reported and methodology used to address the question, we all seem to be on the same page when defining true menopause-related symptoms during the peri- and early postmenopausal years. That is actually very reassuring. We now all agree that there are specific symptoms related directly to the menopause transition that can be severely disruptive of quality of life.

However, my rationale for going into such historic detail is to raise awareness that we still do not seem to get the entire message. The NIH experts concentrated on contemporary treatment of symptoms of menopause, largely suggesting in their review of both prescription and nonprescription marketed products that estrogen or estrogen-progestogen therapy was, in essence, unsafe; that nonhormonal products were not, or were marginally, effective; and that herbal and other related products were as effective as placebo. This approach appears to endorse a medical/disease model of menopause—something the North American Menopause Society (NAMS) does not ascribe to—rather than a health/prevention model, which NAMS does support.

The truth is that a woman’s personal response to the presence of vasomotor-related symptoms is as important as their frequency and severity. That response is influenced by social, cultural, psychological, and environmental factors. For example, some women will stoically tolerate severe vasomotor symptoms while others may be deeply disturbed by mild ones. Even women with identical symptom profiles may react differently to their presence. There is a need to understand the factors that determine this variation in response. We need to come to grips with these aspects; otherwise, we can never truly educate, treat, advise and reassure women about menopause and its true potentially related symptoms. We need to understand that the bottom line for how most women react to menopause symptoms relates to their quality of life in the here and now.

With the acceptance of specific menopause-related symptoms comes the responsibility to treat them, when requested, with the best available therapies. But impediments still block such care. For example, we have in our current society such a defensive attitude toward the few that the majority is invariably left in limbo. Everything in daily life carries a potential risk, but we don’t respond by locking ourselves in a padded cell. It is time, therefore, to reassure women that 1 to 4 years of estrogens used for true menopause-related symptoms in a peri- or early postmenopausal population without adverse risk factors is the treatment of choice, and few experts are in disagreement. Certainly there is some risk associated with estrogens, but the relative risk and the prevalence of the major problems in this age group are low; hence, the absolute risk is extremely low. Moreover, other prescription drugs, such as selective serotonin-reuptake inhibitors, are not as effective, have been only minimally investigated for this indication, and carry their own potential adverse effects. More research will always be necessary, but we have a great deal of data available to us and it is not acceptable for us to debate from a soap box while women are confused, symptomatic, and wanting explanations and relief.

We really need to get beyond this debate in this population, accept that everything in life has pros and cons, and leave it to women to make their own decisions, provided they are well informed and base those decisions on their personal circumstances and quality of life. The current NIH State-of-the-Science Conference Statement offers some glimmer of understanding, but it is hoped that the next conference will move beyond producing yet another summary of what has already been said, and will bring a diverse group of medical and social/behavioral scientists together to try to resolve some of the outstanding questions about menopause. In the meantime, given what we know, it is just not fair to make women feel guilty about taking proven remedies for real symptoms.



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References

1. National Institutes of Health State-of-the-Science Panel. National Institutes of Health State-of-the-Science Conference Statement: Management of menopause-related symptoms. *Ann Intern Med* 2005;142:1003-13.
2. Utian WH. The true clinical features of postmenopause and oophorectomy, and their response to oestrogen therapy. *S Afr Med J* 1972;46:732-7.
3. Utian WH, Serr D. Symptom formation, the climacteric syndrome. In: Van Keep P, Greenblatt R (eds), *Consensus on menopause research*. Lancaster, England: MTP Press, 1976.
4. Dennerstein L, Dudley EC, Hopper JL, et al. A prospective population-based study of menopausal symptoms. *Obstet Gynecol* 2000;96:351-8.