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Hot flashes: behavioral treatments, mechanisms, and relation to sleep

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Hot flashes are the most common symptom of the climacteric and occur in about 75% of perimenopausal and postmenopausal women in Western societies. Although hot flashes accompany the withdrawal of estrogen at menopause, the decline in estrogen levels is not sufficient to explain their occurrence. Elevated sympathetic activation acting through central α_2-adrenergic receptors contributes to the initiation of hot flashes, possibly by narrowing the thermoneutral zone in symptomatic women. Hot flashes are then triggered by small elevations in core body temperature acting within this narrowed zone. A relaxation-based method, paced respiration, has been shown in 3 controlled investigations to significantly reduce objectively measured hot flash occurrence by about 50% with no adverse effects. In 6 studies of physical exercise, however, investigators did not find positive effects on hot flashes, possibly because exercise raises core body temperature, thereby triggering hot flashes. Although many epidemiologic studies have found increased reports of sleep disturbance during the menopausal transition, recent laboratory investigations have not found this effect, nor have they found that hot flashes produce disturbed sleep. Therefore, sleep complaints in women at midlife should not routinely be attributed to hot flashes or to menopause.

Hot flashes are the most common symptom of the climacteric and occur in about 75% of perimenopausal and postmenopausal women in the United States.[1] The frequency of hot flashes can range from 5 per year to 50 per day, with great variations among individuals or even within an individual. They generally persist for 1 to 5 years, but in some women they can continue for as long as 44 years.[2] There is no accepted metric for measuring severity of hot flashes.

Hot flashes are an exaggerated heat dissipation response and comprise widespread cutaneous vasodilation and profuse upper body sweating.[3] They are described as sensations of heat, sweating, flushing, chills, clamminess, and anxiety.[2]

There are few major risk factors for menopausal hot flashes. Two recent investigations[4,5] found that high body mass index (BMI) is directly related to hot flash frequency. This may be caused by the effect of increased insulation from body fat, resulting in elevated core body temperature (T_c), which triggers hot flashes.[6] Cigarette smoking has also been found to increase the risk of hot flashes,[4,5] possibly through the effect on estrogen metabolism or through the thermogenic effects of nicotine.[7]

The opinions offered at the National Institutes of Health (NIH) State-of-the Science Conference on Management of Menopause-Related Symptoms and published herein are not necessarily those of the National Institute on Aging (NIA) and the Office of Medical Applications of Research (OMAR) or any of the cosponsoring institutes, offices, or centers of the NIH. Although the NIA and OMAR organized this meeting, this article is not intended as a statement of Federal guidelines or policy.

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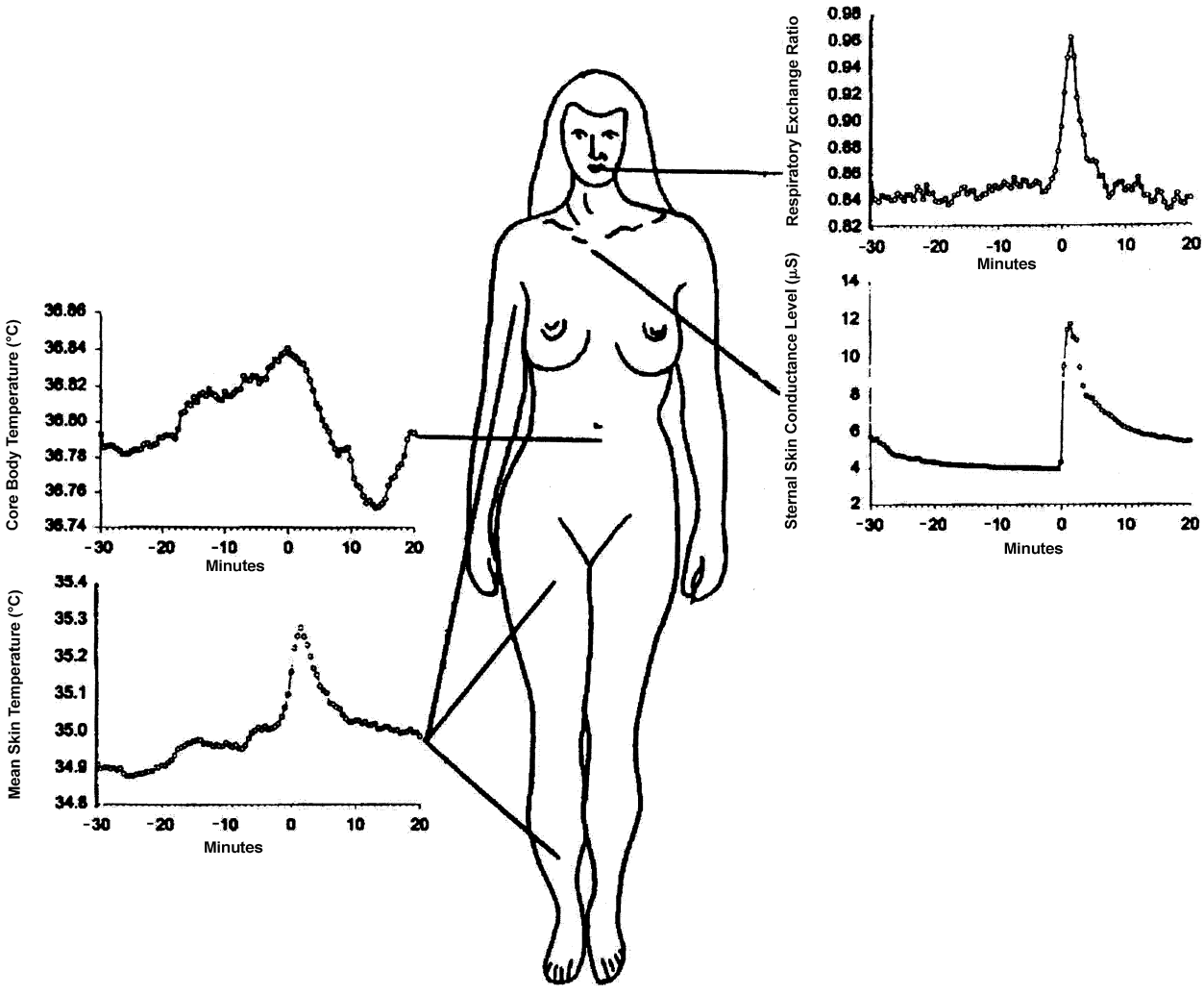

Figure 1 Peripheral physiologic events of the hot flash, based on 29 hot flashes in 14 women. (Adapted from *Fertil Steril*.[8])

Physiologic events of the hot flash

Peripheral vasodilation, demonstrated by increased skin temperature and blood flow, occurs during hot flashes in all body areas that have been investigated (**Figure 1**). Skin temperature increases in the digits, cheek, forehead, upper arm, chest, abdomen, back, calf, and thigh.[8–12] Blood flow in the finger, hand, calf, and forearm also increases during hot flashes.[10–12] These changes typically occur within the first few seconds of the reported onset of the flash.[10]

Sweating and skin conductance, an electrical measure of sweating, also increase during hot flashes. Molnar[9] measured the whole body sweat rate to be about 1.3 g/min in 1 subject. We simultaneously recorded measures of sweating and skin conductance from the sternum during 29 hot flashes in 14 women.[13] There was a close temporal correspondence between both measures that increased significantly. Measurable sweating occurred during 90% of the flashes.

Increased sternal skin conductance has proved to be the best objective marker of menopausal hot flashes to date. A 2-μS increase in conductance measured within 30 seconds corresponded with 95%,[13] 90%,[14] and 80%[15] of patient reports of hot flashes in 4 separate studies. No such responses were recorded in premenopausal or asymptomatic postmenopausal women.[13,14] Measurements of finger temperature and blood flow were less predictive of hot flash occurrence.[15]

The skin conductance measurement is particularly useful for the evaluation of treatment studies because it can be recorded outside the laboratory over prolonged intervals and does not require the patient's intervention. Using the same recording methods with ambulatory monitors, investigators found an 86% agreement between the skin conductance criterion (2 μS/30 sec) and patient event marks.[13] A second study found an agreement rate of 77%.[14] A more recent study using a smaller, solid-state recorder found a concordance rate of 72% in 18 patients with breast cancer who had hot flashes.[16]

Endocrinology of hot flashes

Although hot flashes accompany the withdrawal of estrogen at menopause, the decline in estrogen levels is not sufficient to