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Review

Menopausal hot flashes: Mechanisms, endocrinology, treatment

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ABSTRACT

Hot flashes (HFs) are a rapid and exaggerated heat dissipation response, consisting of profuse sweating, peripheral vasodilation, and feelings of intense, internal heat. They are triggered by small elevations in core body temperature (Tc) acting within a greatly reduced thermoneutral zone, i.e., the Tc region between the upper (sweating) and lower (shivering) thresholds. This is due in part, but not entirely, to estrogen depletion at menopause. Elevated central sympathetic activation, mediated through α_2-adrenergic receptors, is one factor responsible for narrowing of the thermoneutral zone. Procedures which reduce this activation, such as paced respiration and clonidine administration, ameliorate HFs as will peripheral cooling. HFs are responsible for some, but not all, of the sleep disturbance reported during menopause. Recent work calls into question the role of serotonin in HFs.

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Contents

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1. Introduction

Hot flashes (HFs) are the most common symptom of the climacteric and are reported as feelings of intense warmth along with sweating, flushing, and chills. Sweating is generally reported in the face, neck and chest. HFs usually last for 1–5 min, with some lasting as long as an hour [1]. The median duration of symptoms is about four years, with some lasting as long as 20 years [2]. In one U.S. study, 87% of the women reported daily HFs and about a third of those reported more than 10 per day [1]. There is some racial and ethnic variation of HFs with Caucasian women reporting the highest prevalence and Japanese and Chinese women reporting the lowest [3].

2. Physiologic events of the hot flash

Peripheral vasodilation, demonstrated by elevated skin blood flow and temperature, occurs during HFs in all areas that have been studied (Fig. 1). Skin temperature increases in the digits, face, arms, chest, abdomen, back, and legs [4–8] and blood flow in these areas are elevated, as well [6–8].

Sweating and skin conductance, an electrical measure of this, also increases during HFs (Fig. 1D). Molnar [5] determined the whole body sweat rate to be about 1.3 g/min in one subject. We measured sweating and skin conductance from the sternum at the same time in 14 women [4]. We found a close temporal correspondence between both measures, which were significantly elevated. Measurable sweating occurred in 90% of the HFs.

Core body temperature (Tc) also increases prior to HFs. We measured Tc and sternal skin conductance during 77 HFs in 10 menopausal women who reported frequent symptoms [9]. We found small but significant Tc elevations before the majority of HFs and replicated these findings in two subsequent studies [4,10].

The Tc elevations could be caused by increased metabolic rate (heat production) and/or peripheral vasoconstriction (decreased heat loss). We did find significant increases in metabolic rate (Fig. 1B), but they occurred at the same time as the peripheral vasodilation and sweating; peripheral vasoconstriction did not occur. Therefore, the Tc elevations are not caused by metabolic rate elevations. Small increases in heart rate, about 7–15 beats/min do occur along with the metabolic rate increases [5,6].

3. Objective measurement of hot flashes

Typically, diaries are used to assess treatment outcome in HF studies. However, there are several problems with these measures. Errors in compliance are major sources of bias [11]. Also, HFs occurring during sleep are not accurately reported because recall of these events is usually poor and many HFs do not produce awakenings [12]. Finally, placebo effects as large as 40–50% occur with self-reports [13]. Therefore, objective measures of HFs have been developed.

Increased skin conductance recorded from the sternum is presently the best objective marker of HFs. An increase in this measure ≥2 μmho (electrical unit of conductance) within 30 sec corresponded with 95% [14], 90% [15], and 80% of reported HFs [16]. These results have been independently replicated [16]. Moreover, these results have been extended to men with HFs due to androgen depletion by GNRh agonists in the treatment of prostate cancer [17].

The skin conductance measure is also useful because it can be recorded outside the laboratory in daily life. Using the same recording methods with ambulatory monitors, we found an agreement of 85% between the skin conductance criterion and patient event marks [14]. A second study found an agreement of 77% [15].

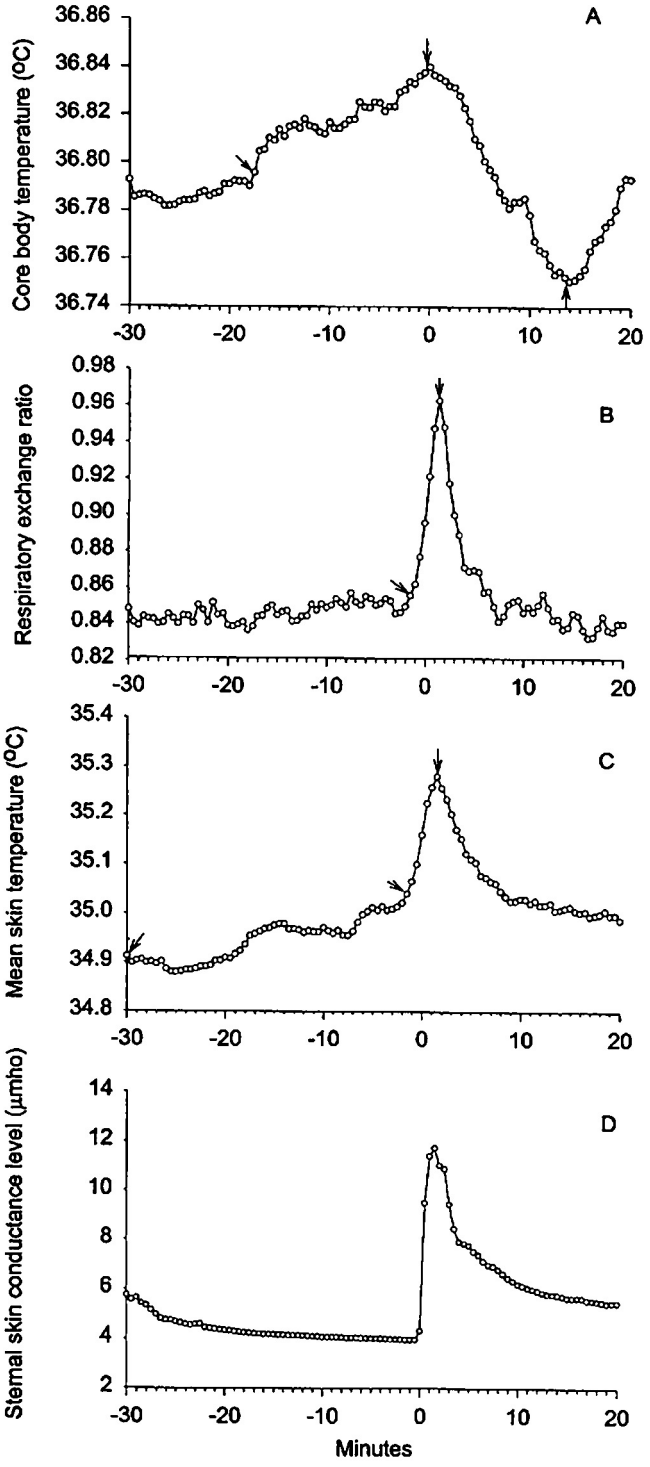

Fig. 1. (A) Core body temperature (means) during menopausal hot flashes. (B) Respiratory exchange ratio (means) during hot flashes. (C) Mean skin temperature (means) during hot flashes. (D) Sternal skin conductance (means) during hot flashes. Time 0 is the beginning of the sternal skin conductance response. Intervals between arrows are significantly different from each other at $P < .05$, Duncan's test.

However, the major drawback of skin conductance recording is that it requires the use of electrodes and gel, which must be changed every 24 h. Therefore, the author has invented a miniature, hygrometric HF recorder (Fig. 2), which requires neither electrodes nor gel [18]. This device will record all HFs for one month using a single hearing aid battery. It attaches to the skin with a