

## PAPERS AND ORIGINALS

## Physiological aspects of menopausal hot flush

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### Summary and conclusions

**Eighteen hot flushes experienced by eight menopausal women were studied and compared with the effects of warming in six premenopausal women. The hot flushes were associated with an acute rise in skin temperature, peripheral vasodilatation, a transient increase in heart rate, fluctuations in the electrocardiographic (ECG) baseline, and a pronounced decrease in skin resistance. Although premenopausal women had greater maximum increases in skin temperature and peripheral vasodilatation, they showed a much smaller decrease in skin resistance and no changes in heart rate or ECG baseline.**

**These findings suggest that the onset of the hot flush is associated with a sudden and transient increase in sympathetic drive. Further investigations may lead to the development of a more specific alternative to oestrogen for relieving menopausal hot flushes.**

### Introduction

Hot flushes are the most common and characteristic symptom of the climacteric, though there is no evidence for a direct relation between circulating oestrogen concentrations and flushes,<sup>1 2</sup> and their aetiology remains obscure. Rather surprisingly the flush has received very little scientific investigation,<sup>3-8</sup> and the rationale for oestrogen treatment has been questioned<sup>6</sup> with some justification. We studied several aspects of the mechanism of the hot flush, including the associated physiological changes.

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### Methods

Eleven menopausal women with an average age of 50.5 years (range 45-54) who were experiencing frequent hot flushes volunteered to take part in the investigation. For comparison six premenopausal women with an average age of 25 years (range 20-35) were also studied at rest and while being warmed by hot-water bottles and blankets.

All the women were seated throughout the study, and the following recordings were begun after a 30-minute rest to allow for stabilisation: single-lead (aVR) electrocardiogram (ECG); digital blood volume pulse by optical plethysmography as a measure of peripheral vasodilatation<sup>7</sup>; skin resistance (ohms) as a reflection of peripheral sympathetic tone<sup>8</sup>; and skin temperature (°C) of hand, arm, and forehead by bead thermistors. The room temperature was maintained at 20°-22°C. Blood pressure was recorded intermittently by mercury sphygmomanometer on three occasions before a flush and at least twice during a flush.

All the results except for blood pressure were expressed as the mean percentage change  $\pm$  SE of mean from the resting value to minimise the effect of individual variations in the absolute measurements. The means were compared by Student's *t* test.

### Results and comment

The results of the study of 18 hot flushes in eight menopausal women and the warming of six premenopausal women are summarised in the table.

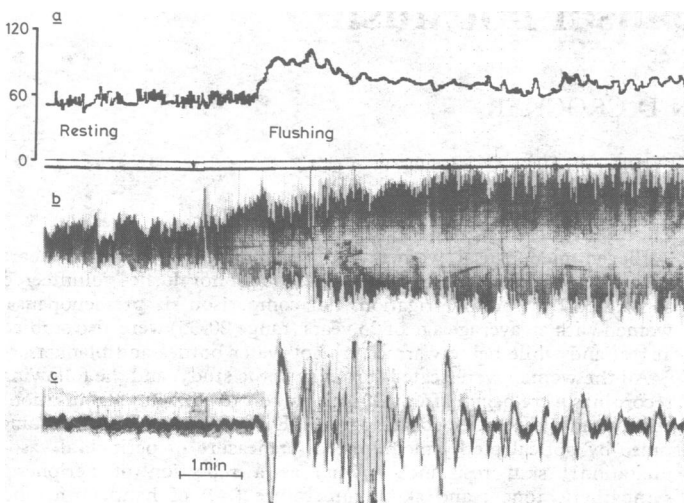
It was difficult to time the flushes accurately, as the end point was usually not well defined. Nevertheless, they varied in duration (approximate range 1-4 minutes) and intensity, and in each case there was an acute rise in the skin temperature of the hand, arm, and forehead which usually coincided with the subjective sensation of flushing. These findings have been confirmed by a separate study using thermography, which showed an average increase of 1°C on the face and neck during flushing.<sup>9</sup> There was a significant ( $P < 0.01$ ) increase in the heart rate at the onset of flushing from a mean of  $71 \pm 3$  to  $86 \pm 4$  beats/min but no change of cardiac rhythm. The ECG baseline, however, fluctuated considerably at the onset of flushing and this coincided with a large increase in the digital blood volume pulse, which persisted. The figure shows these recordings from one menopausal woman. The onset of the flush was also accompanied by an acute fall in skin resistance, and all these changes were also roughly synchronous with the subjective sensation of flushing. No changes in blood pressure were observed during any of the flushes in the first three subjects studied and this measurement was subsequently discontinued.

Warming of the premenopausal women produced much greater skin temperature increases, but there were no changes in heart rate,

Summary of mean ( $\pm$ SE of mean) percentage changes in physiological values during 18 menopausal hot flushes in eight women and warming in six premenopausal women

	Temperature			Heart rate	Digital blood volume pulse	Skin resistance
	Hand	Arm	Forehead			
Menopausal women	2.7 $\pm$ 0.6	2.0 $\pm$ 0.5	2.0 $\pm$ 0.3	21.0 $\pm$ 3.0	157.0 $\pm$ 16.0	-44.0 $\pm$ 6.0
Premenopausal women	8.4 $\pm$ 2.5	8.9 $\pm$ 1.0	4.3 $\pm$ 0.9	0	183.0 $\pm$ 28.9	-8.1 $\pm$ 4.7

ECG baseline, or blood pressure. The digital blood volume pulse, however, increased considerably, which indicated an increased peripheral blood flow due to vasodilatation, but the skin resistance showed only a very small decrease compared with that seen during the hot flushes. All these changes in the premenopausal women depended on the length of warming and were more gradual in onset than the acute changes associated with the hot flush. In contrast, the warming of menopausal subjects provoked hot flushes in all but one woman, whose changes in physiological values were similar to those observed in the premenopausal women.



Physiological recordings of (a) heart rate (beats/min), (b) digital plethysmograph, and (c) ECG from one menopausal woman before and during a hot flush.

## Discussion

The fluctuations of the ECG baseline, increase in heart rate, and changes in skin temperature were similar to the findings in the only other comparable study,<sup>5</sup> but the timing of these changes and of the subjective sensation of the flush were different. Molnar's one subject<sup>6</sup> had no premonition of a flush, though some changes in the physiological recordings were noted before the subjective sensation of flushing. In our subjects the changes in the physiological recordings were often preceded by an indefinable sensation of an impending flush. Occasionally "palpitations" were experienced before or during a flush, but there were no changes in cardiac rhythm. This has been confirmed by a separate study of continuous 24-hour ECG recordings in three other flushing women. Hannan<sup>3</sup> also noted an increased heart rate during flushing, though this was accompanied by an increase in systolic and diastolic blood pressures, which we did not find. Both his and our studies, however, used intermittent measurements, whereas a continuous intra-arterial catheter recording would be preferable.

The subjective sensation of a hot flush seems to be out of proportion to the actual temperature increase of the skin, which was never more than about 1°C. Furthermore, the temperature increase often persisted for several minutes after the sensation of warmth had passed, indicating that the flush is experienced only while the skin temperature is increasing. The severity of the sensation is therefore probably related to the rate of change of temperature as well as to the actual temperature increase.

The vasodilatation in the premenopausal women was not accompanied by changes in heart rate, ECG baseline, or skin resistance comparable to those of a hot flush. Therefore the pronounced changes in these values during hot flushes were not simply a result of vasodilatation or sweating. Skin resistance depends on the total permeability of a selective subcutaneous membrane closely associated with, if not identical to, the eccrine sweat glands.<sup>8</sup> Excitation of the sweat glands by sympathetic cholinergic fibres reduces skin resistance, which is not primarily related to the emergence of sweat.<sup>10</sup> The fall in skin resistance observed at the onset of the hot flush may therefore reflect a sudden increase in sympathetic drive, which is consistent with the observed increase in heart rate. The fluctuations of the ECG baseline are probably due to the change in skin resistance.<sup>11</sup> Since heat-induced vasodilatation of the premenopausal women did not produce these changes in skin resistance, heart rate, and ECG baseline, a sudden and transient rise in sympathetic drive seems to be characteristic of the onset of the menopausal hot flush.

In the hand pulse volume is related to the diameter of cutaneous vessels that are solely innervated by adrenergic fibres,<sup>7</sup> so an increase in sympathetic tone should produce a decrease in pulse volume. Although a decrease was not observed at the onset of the flush, when the changes in ECG baseline, heart rate, and skin resistance were greatest, this may have been because of the short duration of this phase. The persistently increased pulse volume during the flush may result from the local release of a vasodilator factor after an initial acute change in sympathetic tone. This possibility is already under investigation and will be reported later.

Although oestrogen treatment may eliminate hot flushes,<sup>12,13</sup> its potential hazards are well recognised. We hope that improved understanding of the changes associated with the hot flush will lead to the development of a more specific alternative to oestrogen for relieving this distressing symptom.

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