

## Pubertal induction of sweat gland activity

J. REES AND S. SHUSTER

*Department of Dermatology, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 4LP, U.K.*

*(Received 17 October 1980/27 January 1981; accepted 2 February 1981)*

### Summary

1. To study the difference in sweat rate between men and women the rates of cholinergic-induced sweating were measured in normal people before and after puberty and in response to androgens and anti-androgens.

2. Sweat rate in men was more than double that in women.

3. This difference did not occur in prepubertal boys and girls in whom the rate, corrected for surface area, was comparable with that in women.

4. Application or injection of androgen locally did not stimulate sweat production in the adult female.

5. Anti-androgen topically or systemically did not decrease sweat rate in men.

6. It is concluded that the rate of sweat rate in men is caused by androgen-induced gene expression at puberty and not by androgen modulation in adult life.

Key words: androgen, gene expression, puberty, sex difference, sweat.

### Introduction

The convention that men sweat but ladies only perspire corresponds to the observation that the rate of sweating induced by comparable stimuli is greater in men than women. The present study was an attempt to find out why.

### Patients and methods

Sweating was induced on the flexor side of the forearm by iontophoresis of 2% (w/v) pilocarpine

Correspondence: Professor S. Shuster, Department of Dermatology, University of Newcastle upon Tyne, Newcastle NE1 4LP, U.K.

nitrate with a current density of 4 mA for 5 min, which elicits a maximal sweat response. The skin was then dried carefully and an aluminium capsule stuck to the skin with adhesive. Sweat was collected on to 3 cm circles of filter paper placed inside the capsule for 15 min periods and weighed (Johnson & Shuster, 1969). Sweat output was expressed as  $\text{mg h}^{-1} \text{cm}^{-2}$ . In the case of the children the mean sweat rate is also given corrected to adult surface area (average values 1.35 for the boys and girls, 1.9 for the women and  $2.1 \text{ m}^2$  for the men).

The following groups of patients were studied.

(1) Normal men and women. Single measurements of sweat rates were made from the forearms of eight normal adult males and nine normal adult females all within the age range 20–35 years with the exception of one male aged 52 years. (2) Single measurements of sweat rate were also made on the forearms of six normal boys and six normal girls aged 9–10 years from a local primary school. (3) Two experiments were done to study the response to local androgen. In the first experiment 1% (w/v) testosterone propionate in a carbopol/trietholein/ethanol base was applied twice daily for 7 days to one forearm of 12 healthy female volunteer subjects aged 20–35 years and the base alone was applied to the other forearm. On day 7 sweat rates were measured on both forearms. The second experiment was done in two female volunteer subjects aged 25–30 years in whom 0.5 mg of testosterone esters [0.2 ml of a 1:100 dilution of Sustanon 250 (Organon), a sustained-release preparation] was injected intradermally into one forearm and the vehicle alone into the opposite forearm. Seven days later sweat rates were measured at the injection sites on both forearms. (4) The response to anti-androgen was studied after local and systemic administration. In the first experiment

4% (w/v) flutamide (Neri, 1977) in an ethanol-based gel was applied twice daily to one forearm of each of nine normal male subjects aged 25–35 years for 7 days, when sweat rates were measured on both forearms. In the second experiment sweat rates were measured on the forearm before and at weekly intervals during the treatment with cyproterone acetate (100 mg daily) of seven male patients with severe acne.

Fully informed consent was obtainable from all patients and normal subjects and, in the case of the children, also their parents.

## Results

### Normal sweat rates

Sweat rates in the normal adults are shown in Fig. 1; the difference between them is highly significant ( $P < 0.001$ ). Fig. 1 also shows that this difference does not occur before puberty. Sweat rate in the boys and girls was greater than in the adult females, but equal when converted for surface area.

### Effect of androgen

There was no increase in sweat rate in females treated twice daily with topical testosterone propionate (Fig. 2) nor in the two subjects given intradermal testosterone (Table 1).

### Effect of anti-androgen

Conversely, there was no decrease in sweat rate after twice daily application of the anti-androgen flutamide (Fig. 2) to the skin of males; nor was there a significant decrease during systemic administration of cyproterone acetate in the patients treated for acne (Fig. 3).

## Discussion

We have confirmed the well-known sex difference in sweat rate in adults. Since the number of sweat glands is equal in men and women (Szabó, 1962) we conclude that the difference must be due to the secretory capacity per gland. Our new finding that this sex difference does not occur before puberty suggests a puberty related endocrine mechanism. Since the total number of sweat glands is fixed in foetal life, the number of glands/surface area declines progressively with growth into adult life [mean of approximately 3000 glands/cm<sup>2</sup> in a 24 week foetus to 1600 glands/cm<sup>2</sup> at term, to 500 glands/cm<sup>2</sup> at 18 months, to 120 glands/cm<sup>2</sup> in adult life; Szabó

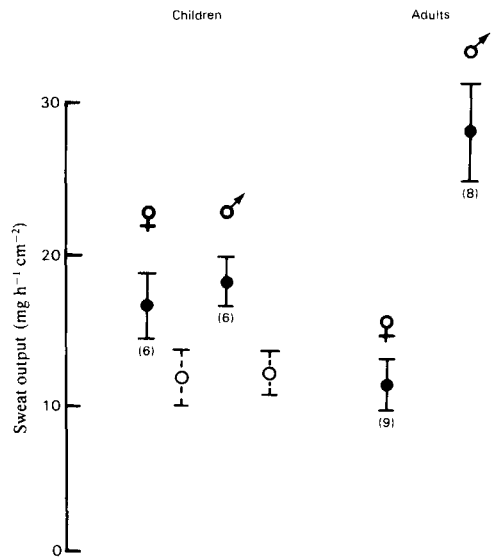


FIG. 1. Sweat rate in boys and girls and in adult men and women. O, Sweat rates in the boys and girls corrected to adult surface area.

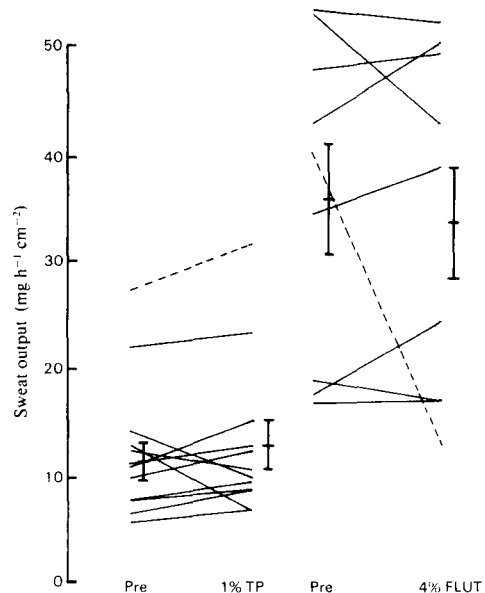


FIG. 2. The lack of effect on sweating of topical testosterone propionate (1% TP) in females and flutamide (4% FLUT) (Pre, prepubertal) in males. ----, Two individuals in whom there was technical doubt about one of the sweat collections.

(1962)] and to compare sweat rate per gland in adults and children a correction has therefore to be made for growth. Thus although sweat rates per surface area were greater in both male and female children than in adult females, when a

TABLE 1. Lack of effect of intradermal testosterone esters on sweat rate in two normal women

Testosterone esters were sustained-release preparations (0.5 mg).

Subject no.	Sweat rate (mg h <sup>-1</sup> cm <sup>-2</sup> )			
	Androgen		Vehicle	
	Before	7 days after	Before	7 days after
1	11.9	14.2	15.3	17.5
2	19.8	19.8	19.8	18.1

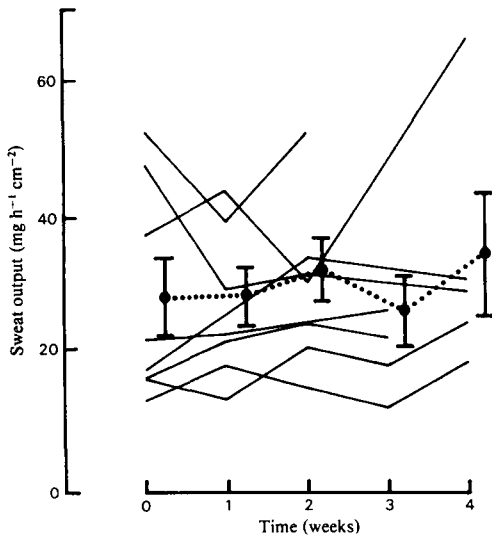


FIG. 3. The lack of effect of oral cyproterone acetate on sweat rate in patients with acne.

surface area correction was applied, the rates were comparable in children and adult females suggesting an equal output per gland with an increase in males after puberty.

A major factor in sweat gland response is work load and sweat gland training; a difference in physical activity after puberty could therefore contribute to the sex difference in sweat rate. This would not, however, explain the difference in the subjects we studied who were comparable both in work and leisure activity; nor would it explain the increase in sweat rate which we have found in women with primary cutaneous virilism (Shuster, 1972) or idiopathic hirsutism (Burton, Johnson, Libman & Shuster, 1972) in otherwise normally feminine women. Thus the likely explanation of the pubertal increase in sweat rate is the endocrine effects of puberty. Preliminary observations (J. Rees & S. Shuster, unpublished work)

are that the increase does not occur in adults with eunuchoidism of prepubertal origin, which suggests that the factor responsible is gonadal androgen. Despite this, the sweat glands did not respond to local androgens in the female nor to local and systemic anti-androgens in the male. In the case of the topical agents used there is independent evidence of adequate absorption from studies of sebaceous gland function (F. Lyons, J. Frazer & S. Shuster, unpublished work; Lutsky, Budak, Cozill, Monahan & Neri, 1975); moreover there was no response to androgen injected directly into the skin nor to systemic cyproterone acetate in doses known to be effective in the skin and which in the same patients had decreased sebum excretion rate by up to two-thirds by week 4 of the study (F. Lyons & S. Shuster, unpublished work). We therefore conclude that although the difference in sweat rate between males and females is initiated by androgen at puberty it is not maintained by androgen. Thus the probable mechanism is by androgen-induced gene expression. We have demonstrated a similar mechanism in the sebaceous gland of the rat for both gonadal hormones and  $\alpha$ -melanocyte-stimulating hormone ( $\alpha$ -MSH) (Thody & Shuster, 1971; Shuster & Thody, 1974; Shuster, Hinks & Thody, 1977; Thody, Meddis & Shuster, 1978) and Toh (1979) has found a similar action for thyroid hormones. The possibility that certain endocrine changes in the skin are due to gene expression during a critical stage of development, rather than to continuous action of hormones, has important implications for the aetiology and treatment of disorders such as acne and cutaneous virilism (Burton *et al.*, 1972; Shuster, 1972), since it is unlikely that even a totally effective anti-androgen will cure the condition.

**Acknowledgment**

We are grateful to Mr L. Chadwick for technical assistance.

**References**

BURTON, J.L., JOHNSON, C., LIBMAN, L. & SHUSTER, S. (1972) Skin virilism in women with hirsutism. *Journal of Endocrinology*, **53**, 349-354.  
 JOHNSON, C. & SHUSTER, S. (1969) Eccrine sweating in psoriasis. *British Journal of Dermatology*, **81**, 119-124.  
 LUTSKY, E.M., BUDAK, M., COZILL, P., MONAHAN, M. & NERI, R.O. (1975) The effects of a non-steroidal antiandrogen, flutamide, on sebaceous gland activity. *Journal of Investigative Dermatology*, **64**, 412-417.  
 NERI, R.O. (1977) Studies in the biology and mechanism of action of nonsteroidal antiandrogens. In: *Androgens and Antiandrogens*, pp. 179-189. Ed. Martin, L. & Molla, M. Raven Press, New York.  
 SHUSTER, S. (1972) Primary cutaneous virilism or idiopathic hirsuties. *British Medical Journal*, **ii**, 285-286.

- SHUSTER, S. & THODY, A. J. (1974) The control and measurement of sebum secretion. *Journal of Investigative Dermatology*, **62**, 172-190.
- SHUSTER, S., HINKS, W.M. & THODY, A.J. (1977) The effect of sex and age of gonadectomy on the sebaceous response to progesterone. *Journal of Endocrinology*, **73**, 67-70.
- SZABÓ, G. (1962) The number of eccrine sweat glands in human skin. *Advances in Biology of Skin*, **3**, 1-5.
- THODY, A.J. & SHUSTER, S. (1971) Increased sebum secretion in adult female rats after neonatal treatment with testosterone propionate. *Journal of Endocrinology*, **49**, 677-681.
- THODY, A.J., MEDDIS, D. & SHUSTER, S. (1978) Increased sebaceous gland activity in the adult rat after  $\alpha$ -melanocyte-stimulating hormone treatment during early life. *Journal of Investigative Dermatology*, **70**, 328-330.
- TOH, Y.C. (1979) Effect of neonatal administration of thyroxine on the rate of sebum production in rats. *Journal of Endocrinology*, **83**, 199-203.