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Effect of Lipid Solvents on Cutaneous Moisture Loss

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Abstract

Application of various lipid solvents and dimethyl sulphoxide to the skin of cattle, sheep, eland and African buffalo exposed to an air temperature of 20°C caused an increase in cutaneous moisture loss.

The effect did not occur after exposure to an air temperature of 40°C or after adrenaline administration.

Blockage of sweating by either bethanidine or phenoxybenzamine did not affect the response.

Camel, donkey, dog and man showed no increase in cutaneous moisture loss after lipid solvent application to the skin.

It is concluded that lipid solvents directly stimulate the secretory cells of the sweat glands of members of the family Bovidae and that this is not due to the release of transmitter substance nor to stimulation of adrenergic receptors, but is due to direct stimulation of the sweat glands themselves.

Introduction

It was noted by one of us (Y.S.P.) that the application of diethyl ether to the skin of cattle caused an increase in cutaneous moisture loss. This finding has been investigated to ascertain if the increase is due to (1) an increase in the rate of water diffusion through the skin as has been previously demonstrated (Sweeney and Downing 1970), or (2) stimulation of the sweat glands. The study has been extended to other species of the family Bovidae and to some non-bovid species. Also, a variety of other lipid solvents have been tested, and in addition, dimethyl sulphoxide, a substance noted for powers of skin penetration.

Materials and Methods

Experimental Animals

The cattle used were Brahman and zebu bulls or steers (*Bos indicus*) and Hereford × Shorthorn bulls (*Bos taurus*).

The sheep (*Ovis aries*) were of the Merino breed. One male eland (*Taurotragus oryx*) and one female African buffalo (*Syncerus caffer*) were also used.

The non-bovid species were donkey (*Equus asinus*), camel (*Camelus dromedarius*), dog (*Canis familiaris*) and man (*Homo sapiens*).

Measurement of Cutaneous Moisture Loss

Cutaneous moisture loss was qualitatively recorded using a ventilated capsule (McLean 1963). The method involves measuring the difference in wet-bulb temperature of two streams of air, one being drawn through the capsule and the other by-passing the capsule.

In the field experiments on eland and buffalo, a quantitative desiccant capsule method with anhydrous calcium sulphate as the desiccant was used (Taylor and Lyman 1967).

Drug Administration

Lipid solvents were applied to the skin using cotton wool, and measurements made immediately afterwards. Evaporation of the solvent from the skin surface does not interfere with the method for the measurement of cutaneous moisture loss. Solvents used were diethyl ether, acetone, benzene, ethyl alcohol, dichloromethane, carbon tetrachloride, and dimethyl sulphoxide.

Drugs were injected intravenously as single shots through a polythene cannula which was inserted aseptically into either the right or left jugular vein before the experiment. Drugs administered in this manner were phenoxybenzamine hydrochloride, bethanidine sulphate, and adrenaline hydrochloride.

Experimental Procedure

Experiments were performed in a climatic room at air temperatures of either 20 or 40°C and at a vapour pressure of approximately 10 mm Hg. Experiments on eland, buffalo, and camel were performed outside on lightly restrained animals at air temperatures of approximately 20°C. Experiments on cattle were carried out at Liverpool, New South Wales, and Rockhampton, Queensland, Australia, and those on other species at Nairobi, Kenya.

Results

Cattle

(i) *Effects of ether*

At environmental temperatures of 20°C ether application to the skin produced an increase in cutaneous moisture loss which persisted for between 12 and 24 h. If ether was applied a second time to the skin after the evaporative loss had reached its maximum level then no further increase occurred. If, however, ether was applied as the evaporative loss was declining then cutaneous moisture loss increased to its previous highest level.

At an environmental temperature of 40°C ether had no effect on cutaneous moisture loss.

(ii) *Effects of other lipid solvents*

Other solvents tested were acetone, alcohol, benzene, carbon tetrachloride, dichloromethane and dimethyl sulphoxide. All substances produced essentially similar results except that carbon tetrachloride produced a response less than the other solvents. Application of ether after carbon tetrachloride caused a further increase in cutaneous moisture loss to a level similar to that produced by the other solvents.

(iii) *Effects of drugs*

Intravenous administration of adrenaline (2·5 μg/kg body weight) to an animal exposed to an air temperature of 20°C caused an increase in cutaneous moisture loss; subsequent application of ether to the skin had no effect on cutaneous moisture loss. Similarly, if ether was applied locally to an area of skin followed by intravenous adrenaline administration then no effect on the ether-induced response was observed, although an untreated area showed a marked increase in cutaneous moisture loss (Fig. 1).

Intravenous administration of bethanidine sulphate (1 mg/kg body weight) 1 h before exposure to an air temperature of 40°C inhibited the heat-induced but not the

adrenaline-induced increase in cutaneous moisture loss. If, 1 h after exposure to heat, ether or other lipid solvents were applied to an area of skin, there was an increase in moisture loss localized to the area of application.

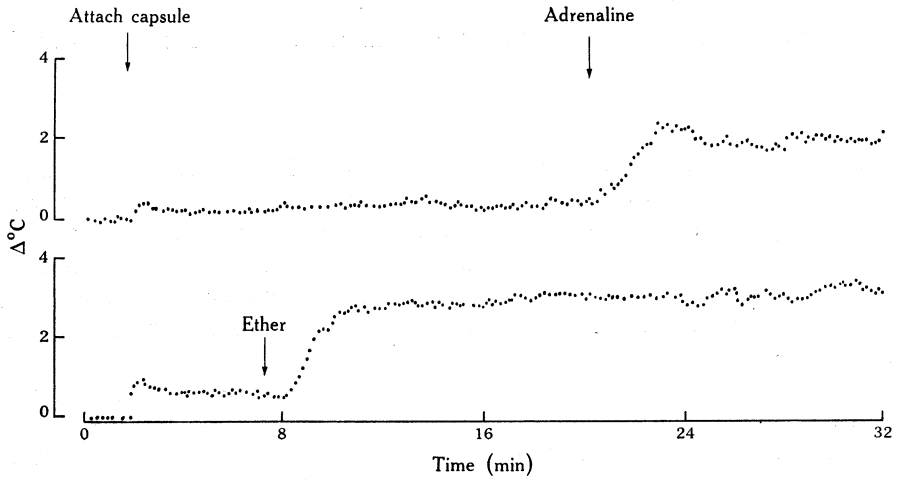

Fig. 1. Simultaneous records of cutaneous moisture loss from two regions of the skin of a bull exposed to an air temperature of 20°C. In the lower record ether was locally applied to the skin under the capsule as indicated by the arrow. The upper record was the control area and demonstrates the effect of the intravenous administration of adrenaline (2·5 μg/kg); adrenaline had no effect on the ether-treated area. Δ°C is the difference in wet-bulb temperature of the air being drawn through the capsule (flow rate 1·2 litre/min) and room air.

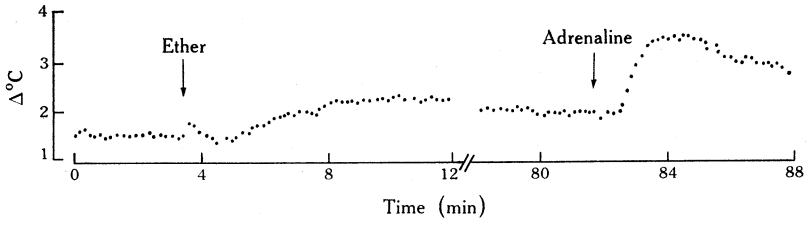

Fig. 2. Cutaneous moisture loss from the skin of a sheep showing the effects of the local application of ether followed by the intravenous administration of adrenaline (3 μg/kg). Ordinate as in Fig. 1.

Intravenous administration of phenoxybenzamine hydrochloride (3 mg/kg body weight) 1 h before exposure to an air temperature of 40°C inhibited both heat-induced and adrenaline-induced sweating. Lipid solvents, however, were still able to produce an increase in cutaneous moisture loss 1 h after the animal was exposed to heat.

Sheep

In contrast to cattle, the application of ether to the skin of sheep caused an increase in cutaneous moisture loss which persisted for 2 or 3 h. Intravenous injection of adrenaline (3 μg/kg body weight) caused a further transient increase in evaporative loss (Fig. 2).

Eland and Buffalo

In both these species ether caused an increase in cutaneous moisture loss.

Camel, Donkey, Dog and Man

In all these species ether failed to cause an increase in cutaneous moisture loss.

Discussion

It is known that the application of lipid solvents to skin *in vitro* increases the rate of diffusion of water through skin. Likewise, dimethyl sulphoxide has a similar effect although its lipid solvent action is minimal (Sweeney and Downing 1970). Thus, the lipids of the epidermis represent to some degree a barrier to the transepidermal diffusion of water. This does not seem to be the explanation for the effect of lipid solvents on cutaneous moisture loss reported here. The evidence suggests a direct action on the sweat glands.

It is considered that the increase in cutaneous moisture loss caused by heat exposure or intravenous adrenaline administration is due to stimulation of the sweat glands (Findlay and Robertshaw 1965). Either exposure to an air temperature of 40°C or a single intravenous injection of adrenaline (2·5 μg/kg) will produce maximum sweating in cattle (Robertshaw, unpublished data). Since, in cattle, lipid solvents had no effect on cutaneous moisture loss after the maximal stimulation of sweating by heat exposure and since adrenaline did not increase cutaneous moisture loss after the application of lipid solvents, it would seem that the lipid solvents produce their effect by sweat gland stimulation. If the lipid solvent effect was due to an increase in transepidermal diffusion then it might be expected that intravenous adrenaline administration would result in a further increase in cutaneous moisture loss due to sweat gland stimulation. This was not the case, which lends further support to the conclusion that the sweat glands have been stimulated.

The experiments using the autonomic blocking drugs were designed to elucidate the possible mechanism whereby the lipid solvents stimulate the sweat glands. Sweating in cattle is controlled by an adrenergic mechanism mediated by α-receptors. Bethanidine blocks the release of adrenergic transmitter to the sweat glands and phenoxybenzamine blocks the receptor site (Findlay and Robertshaw 1965). Neither drug, although they both blocked the sweat response to heat exposure, suppressed the effect of lipid solvents. It would seem, therefore, that the solvents are not acting by stimulating the release of transmitter from conductor nerve endings or by directly stimulating the receptors. They must, therefore, act directly on the secretory cells and cause sweat secretion. Another component of the secretory process is the expulsion of the contents of the sweat gland lumen by the contraction of the myoepithelial cells. This is well illustrated in the sheep and goat where sweat gland response to heat exposure consists of a series of discharges of moisture on to the skin surface. Robertshaw (1968) concluded that in the sheep and goat intravenous adrenaline administration stimulated both myoepithelial contraction and active sweat secretion. In the present experiments adrenaline was able to induce, in sheep, the further expulsion of sweat after the application of ether to the skin, ether causing a small rise in cutaneous moisture loss (Fig. 2). This suggests that ether affects only the secretory and not the myoepithelial cells.

Only domestic and feral members of the family Bovidae showed a sudorific response to lipid solvents. When compared with other species that show thermoregulatory sweating the family Bovidae have a unique system of sudomotor control (Robertshaw 1971) and the phenomenon described here is also confined to this family in that the camel, donkey, dog and man show no response to lipid solvents.

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