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Measurement and control of perspiration

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Synopsis—A short description of the ECCRINE and APOCRINE SWEAT GLANDS is given. Methods available for visualizing sweat on the SKIN, and for collecting and measuring the quantity produced, are reviewed. Brief mention is made of factors which can influence sweating, materials which have been used to inhibit sweating and the MECHANISMS by which they function.

Introduction

Under conditions of extreme emotional, sensory, or thermal stress the response of the human body is strikingly evident in the form of beads of moisture which appear on the skin surface. This moisture, or perspiration, is the product of the two to three million skin structures which collectively are referred to as the 'sweat glands', but individually are identified as either eccrine or apocrine glands.

Eccrine sweat glands

The eccrine glands are tubular, coiled structures 0.4 mm in diameter (1) extending into the subdermal fat and opening on to the skin surface via

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their own duct orifice (2). Spearman (3) has demonstrated that a minority of eccrine glands are twin glands with a common terminal excretory duct.

Functional from the age of 2½ years, the eccrine glands are distributed over the whole body surface, and are concerned with the regulation of body temperature by the evaporation of sweat from the skin surface.

Eccrine secretion is a clear fluid (pH 4.0-6.0) consisting of 99.0-99.5% water and 0.5-1.0% solids, a mixture of inorganic salts, largely sodium chloride, and organic substances which include lactic acid and traces of urea (4).

Apocrine sweat glands

The apocrine sweat glands, which become functional at puberty, are phylogenetically much older than the eccrine glands, but in man this gland system has become rudimentary and distribution is largely confined to the axillae, breasts and urogenital areas. The apocrine glands are derived from the follicular epithelium and generally are associated with a hair although not all hair follicles possess them (1, 5, 6). Like eccrine glands they are coiled structures, but larger, 4.0 mm in diameter (1). Their secretion, which fluoresces, is a turbid fluid (pH 5.0–6.5) containing proteins, reducing sugars, ferric iron, and ammonia (5, 6).

Response of sweat glands to external stimuli

The sweating response provoked by sensory and emotional stimuli, and that elicited by thermal stimulation exhibit considerable variation (7, 8): maximal emotional sweating occurs on the palms and soles whilst maximal thermal sweating is seen on the fingers, arms, forehead and axillae (9). The eccrine glands of the axillae respond to emotional as well as to thermal stimuli.

Below a certain 'critical' temperature (31–32°C) only microscopic amounts of sweat are visible on the skin. This 'insensible perspiration' results from periodic activity of groups of eccrine glands (10), and in a temperate climate is estimated to average about 4.2 mg cm^{-2} h^{-1} (11). Above this 'critical' level, a sudden increase in sweating occurs: this is termed 'reflex sweating' and with this type of response the output of a single eccrine gland on the arm or leg is between 0.222 and 0.258 mg h^{-1} (12).

Apocrine glands respond to emotional and sensory stimuli only and, in comparison with eccrine secretion, the quantity of apocrine secretion is minute. Following stimulation a single axillary apocrine gland produces 0.001 ml fluid and then is unable to respond again for at least 24 h (5, 6).

In the axilla the number of eccrine glands is four to five times that of apocrine glands (6); thus in this region eccrine secretion must obviously predominate. In man the presence of clothing limits the evaporation of sweat from the skin surface and, in the axillae in particular, the absorption of sweat by clothing can be uncomfortable, unsightly and frequently deleterious to fabrics. This combination of factors has given rise to the cosmetic manufacturer's interest in the sweat glands, and his attempts to develop products which will diminish the production of sweat in the axillae. This in turn necessitates the use of techniques by which sweat gland activity can be observed and measured, so that the efficacy of possible antiperspirant materials can be assessed.

Observation and measurement of sweat gland activity and assessment of antiperspirant effect

In vitro methods

These methods of testing antiperspirant materials at best only give an indication of relative effectiveness and the systems used bear little or no resemblance to the human skin. The few methods that have been devised are based upon the fact that many antiperspirant materials, particularly aluminium salts, are astringent, i.e. they are capable of denaturing proteins.

Protein precipitation

Govette and Navarre (13) utilized protein precipitation from egg albumin as a rapid test for astringency. The amount of precipitation, assessed visually, was considered to be proportional to astringency and therefore to antiperspirant activity.

Shrinkage and permeability of frog skin

The same authors used the degree of shrinkage of frog skin as a measure of astringency, whilst Ukrami and Christian (14) developed a test for antiperspirants based upon the observation (15) that iodide and sodium ion

permeability of frog skin increased after treatment with aluminium salt astringents. The complete antiperspirant product was applied to the dorsal skin of frogs; 1 h later skin samples were removed and the extent of iodide penetration from a radio-active solution was determined.

In vivo methods

Cats (16-19), rats (19-21), and mice (21), have been used for studies of sweating, but the sweat glands in these species are confined to the foot-pads and although they are eccrine glands they differ histologically from those of man. *In vivo* studies involving the human eccrine sweat gland system are obviously preferable and investigation of all aspects of sweat glands and their function has resulted in a variety of techniques for visualizing, assessing and collecting sweat. Some of these methods are purely qualitative, others are quantitative or semi-quantitative.

Stimulation of eccrine sweat glands for experimental studies

Excitation of the glands is a prerequisite of studies on sweat gland function since the resting secretion is small and consequently difficult to measure; under such conditions inhibition would be even more difficult to assess.

Stimulation has been achieved by administration of 0.5-1.0 g acetylsalicylic acid, followed by the intake of copious quantities of hot tea (22). More recently, injection of cholinergic compounds such as acetyl choline, mecholyl, carbachol, or pilocarpine (23, 24) has been found to induce sweating, and is frequently used in sweat gland studies.

Although exercise and application of local heat (23) promote a response, one of the most useful methods of inducing sweating is to place the subject in a warm room, or chamber (23, 25-28). Recommendations of different authors for values to be maintained in such a room vary considerably, but generally are within the range 32-40°C and 40-80% relative humidity. Studies of axillary perspiration are most conveniently carried out under such conditions. After entering a warm environment there is generally a latent period before perspiration increases (29) and so the subject is allowed to reach equilibrium with his surroundings before measurements are taken.

VISUALIZATION OF SWEAT AND THE SWEAT DUCT ORIFICE

Colorimetric techniques

Although the presence of sweat can be observed with the unaided eye, or by use of an otoscope or dissecting microscope (5) determination of the numbers of sweat glands and semi-quantitation of sweat is more readily carried out if use is made of a chemical reaction involving a colour change. The intensity and extent of the colour change provides an indication of the amount of sweat produced. In these methods the solutions are painted directly on to the skin and solubilization of the reagents by sweat effects a colour change.

The well-known starch-iodine test devised by Minor in 1927 (22, 30) was one of the earliest colorimetric methods and gave blue-black coloration at the site of sweating. Since then there have been modifications of the method (31, 32) which permits extremely small quantities of sweat to be seen with the naked eye. In place of iodine Guttmann (33) used the sodium salt of chinazarin 2-6-disulphonic acid.

Comparison of the effects of different treatments on the same group of glands has been achieved by preparing black and white positive transparencies from photographs of the treated site (visualized by the starch-iodine method) and then superimposing these transparencies (34).

Other indicators used have been saturated alcoholic cobalt chloride which gives a colour change from blue to bright pink (35), phenolphthalein which goes deep red in contact with sweat (36), a suspension of bromophenol blue in silicone (37), and a 5% solution of o-phthaldialdehyde in xylene which gives a black stain when it comes into contact with the ammonia present in sweat (38).

Although most of the stains used in these procedures can be washed off the skin, some of them are more permanent and several workers have adapted the starch-iodine method, or devised other methods, which allow the colour reaction to develop away from the skin. These methods have the added advantage that they provide 'prints' of the sweat pore pattern and can be used on dark-skinned subjects. Randall (23) used iodine on the skin in conjunction with a starch-containing paper; Papa (39) exposed a paper towel to iodine vapours after it had been in contact with skin painted with a starch-castor oil mixture.

Silverman and Powell (40) reacted a 25% solution of ferric chloride, painted on the skin, with a paper which had been soaked in 5% tannic acid

solution; the grey-blue to blue-black colour reaction represented sites of active sweat gland secretion.

A paper which had been in contact with the sweating skin was treated with a 10% silver nitrate solution and the resulting precipitated silver chloride, when reduced by uv light, provided a picture of the sweating pattern (41).

Plastic impressions and replicas

Impressions of the skin have been obtained by use of a 2–4% solution of polyvinyl formal in ethylene dichloride containing 1% butyl phthalate as plasticizer. Viewed microscopically, holes seen in the plastic film corresponded to the sites of sweat duct orifices (42).

Sarkany (43) used *Siflo Dental Plastic* to produce a skin impression. Metal shadowing of a replica taken from the impression allowed the sweat duct orifices to be seen under the microscope. Alternatively an impression obtained in this manner has been treated with silver nitrate: reduction of the precipitated silver chloride made the sites of sweat secretion visible (45).

Hygrophotography

This is a system based on the reversible colour changes which a silver-mercuric-iodide salt undergoes when exposed to the consecutive effects of light and humidity (44). An orthochromatic photographic emulsion is treated successively with a metol-hydroquinone developer, sodium thiosulphate, mercuric chloride and potassium iodide. The end result is a yellow film which is then blackened by exposure to light. If this blackened plate is put into contact with sweating skin a reversible colour change occurs and the sweat droplets produce a yellow pattern.

Gravimetric techniques

Visual methods of assessing sweat secretion are both useful and adequate for evaluating numbers of glands, or for assessing antiperspirant products where an 'all-or-nothing' effect is sought (as in the case of anticholinergic agents). However, most of the available materials only partially inhibit sweat production and often relatively fine distinctions need to be made between experimental products: in these cases fully quantitative techniques are required.

Capillary collection methods

These methods have been described (5, 46) but are really only of interest if small quantitites of sweat are needed for analysis, as only single glands are studied.

Collection chambers

Collection devices attached to the skin have been used by several workers. Basically, these consist of a ring, with a flange which supports a disc of pre-weighed filter paper (2.5 cm diameter) and a close-fitting cover to prevent evaporation of sweat absorbed by the paper. The open side of the chamber is held in contact with the skin by straps, or by cement (*Duco Household Cement, Durofast, Weldwood Contact Cement*). If cemented to the skin the collection device can remain in position for 2-3 days. Quantities of about 0.01-0.1 ml of sweat can be absorbed on the filter paper discs and collections are usually made over a period of 10-30 min. Schwartz, Thaysen and Dole (47) used an aluminiun unit in preference to an earlier plastic unit which warped on repeated usage (48). One of the problems encountered with this method is leakage of sweat into the collection area from the surrounding areas; Sato and Dobson (49) overcame this by the design of a chamber which had a knife edge to contain sweat in the collection area and drainage grooves in the base to drain sweat in the surrounding areas away from the collection site.

Such methods, whilst being convenient as a means of collecting sweat for chemical analysis, present problems if considered as routine test methods. Ideally the axillae should be utilized for collections as this is the site in which the antiperspirant product is expected to exert its inhibiting effect in practical usage. The shape of the axillary vault makes the attachment of collection devices difficult and the time required for a cement to dry may be as long as 20 min.

Absorbent pads

A gravimetric method which has found favour (29) on account of its simplicity of operation is the 'pad' method. Tared, absorbent cotton pads, about 65 $\times$ 140 mm in size, fit comfortably into the axillae and the quantity of sweat produced in a given time is readily determined. MacMillan, Reller and Synder (26) left the pads in position for 10 min and then immediately transferred them to tared, covered, containers and placed fresh pads in the axillae for a further 10 min. Control sweat collections were generally made

during a 2-week period before antiperspirant treatment was started. Stoughton, Chiu, Fritsch and Nurse (25) utilized 30-min collection periods.

The pad method has proved to be extremely useful for the assessment of axillary sweating and despite the possible errors inherent in the technique (weighing errors, evaporative loss from the pads, lack of distinction between sweat and sebum, variation in position of the pad in the axillary vault) it is widely used as a routine technique for testing antiperspirant products.

In testing antiperspirants it is usual to take 'control' collections during a period when neither axilla is being treated; in the ensuing period the antiperspirant under test is applied to one axilla only, the other remaining untreated. Generally, the axilla in which sweating is most profuse receives applications of the test antiperspirant.

To interpret the results of such tests, it is necessary to know (and possibly to standardize) the amount of antiperspirant material applied to the skin, either as a total dose or as a dose per unit area of skin, along with the time interval between application of test material and measurement of inhibition.

Treatment of results

Frequently the weight of sweat produced in each axilla is totalled and the average ratio of one axillary total to the other is determined. The percentage reduction in sweating caused by application of antiperspirant is calculated:

$$1 - \frac{\text{Treatment week ratio}}{\text{Ratio prior to treatment}} \times 100 \qquad (27)$$

Wooding (50), however, suggests that in gravimetric tests on axillary sweating the geometric mean, rather than the arithmetic mean, should be used in the calculation; in this case all the weights should be converted into the natural logarithms prior to statistical analysis being carried out.

INSTRUMENTAL TECHNIQUES

In the last 20 years precision instrumental techniques have been developed for quantifying sweat gland activity. These methods mostly involve the use of a collection chamber attached to the skin surface through which a stream of dry gas, or gas with a known low relative humidity (RH),

is passed. The moisture picked up by the gas as it passes through the collection chamber represents the moisture lost from the enclosed skin area. The gas used is generally air, oxygen, or nitrogen and the moisture collected by this stream of gas can be measured in one of the following ways:

(i) gravimetrically, following condensation in a collection coil (8, 27, 29, 51-54).

(ii) by humidity-sensing elements which undergo conductivity or resistance changes with variations in the RH of air passing over them (17, 52, 53, 56-58).

(iii) by absorption of infra-red radiation (59, 60).

Collection coils

Kuno (8) used a celluloid collection chamber through which gas dried by passing over calcium chloride or phosphoric anhydride was passed. Moisture picked up by the gas stream was trapped in tared U-tubes filled with calcium chloride. In place of such U-tubes, Pinson (51) used flasks containing pumice stone saturated with concentrated sulphuric acid.

Since cellulose acetate allows slow diffusion of water Neumann, Cohn and Burch (52) used a brass collecting chamber and aluminium coils immersed in an alcohol-dry ice freezing mixture as this was considered more effective in removing the moisture than calcium chloride. The authors claimed that this method had an accuracy of 2.6%.

Jenkins (27) published a similar method, but collections were carried out in the axillae where metal cups were held in position with rubber straps. An air flow of 1.8-2.2 l min^{-1} was considered adequate for complete removal of moisture from each axilla, whilst still allowing complete condensation in the coils.

Often in these tests the mass of sweat collected is only a fraction of the mass of the coil, and great care must be taken in measurement. The coils must be thoroughly dry inside and out when their mass is first determined and before the subsequent determination is made they must be dried on the outside and any air in them brought to atmospheric pressure.

Humidity sensing elements

These elements generally consist of a small plate coated with a thin film of a material whose electrical conductivity (or resistance) varies in proportion to the moisture-content of a stream of air passing over it. When used in perspiration studies, air from a collection chamber attached to the

skin is passed over the sensing element and changes in the conductivity of the surface of the element (which reflects changes in the sweat output of the skin area enclosed by the collection chamber) are monitored and displayed by electronic recording instruments.

A variety of transducing systems have been employed in sensing elements and some of those mentioned in the literature are listed below:

1. Changes in resistance of a sodium chloride crystal (55), which proved unsatisfactory because of lack of standardization (52).
2. A hygroscopic plant pith whose resistance changed with vapour pressure (56).
3. Dissociation of lithium sulphate (53).
4. A thin film of hygroscopic lithium chloride (56).
5. A layer of phosphorus pentoxide between two platinum wires (53).
6. Changes in resistance of a coating of carbon on a polystyrene plate (53, 57).

In practice, several elements may be used for detecting changes in sweating rates. For example Bullard (56) generally used one wide-range element covering the RH range of 5-40%, and up to six narrow-range elements each covering a different RH range, in steps of 9-12%, and could switch from one element to another. Changes in resistance of the elements were displayed on a strip-chart recorder.

With these methods the rate of air flow is of paramount importance; the flow rate and relative humidity must be adequate to ensure complete and rapid evaporation of moisture without causing local cooling of the skin which might inhibit sweating. In order that the air passing through the collection chamber did not become saturated Bullard (56) used a sufficiently high flow-rate to ensure that the effluent RH did not exceed 30%.

When using humidity sensing elements calibration of the elements is essential. From the calibration curves the relative humidity values of the air emerging from the collection chamber can be determined. Using these values the amount of water evaporated from the skin can be calculated from the relative humidity change (ΔRH) in the gas as it passed over the skin surface, from the air flow, and from the temperature:

$$\underset{(\text{mg min}^{-1})}{\text{Sweating rate}} = \underset{(\text{l min}^{-1})}{\text{Air flow}} \times \frac{\Delta\text{RH}}{100} \times \underset{(\text{mg l}^{-1})}{\text{Density of saturated steam}}$$

(The density of saturated steam at the temperature of the experiment can be obtained from Handbook Tables).

A correction for surface area may be applied if required.

Instead of having a constant air flow and monitoring changes in relative humidity, a predetermined constant RH can be maintained in the collection chamber by varying the air flow (58). The humidity sensing element forms part of a Wheatstone bridge; sweat present in the air current alters the resistance of the element and unbalances the bridge. The signal resulting from this imbalance is used to regulate dry air flow and so restore the RH in the collection chamber to its original level. This technique is claimed to be extremely sensitive and capable of detecting an increase in sweating of the order of 0.08 mg within the chamber and the authors claim that the system can be used in the axillae.

Galvanic skin resistance

The galvanic skin resistance has been used to measure the sweat gland activity in rats (19), and Bettley and Grice (53) used it to indicate the presence of sweating within a collection chamber attached to the skin. However, although the galvanic skin resistance largely depends on sweat secretion, it also varies with changes in vascularization of the skin, and is not a specific indicator of sweat secretion (9).

Absorption of infra-red radiation

An entirely different approach to the quantification of sweating rates has arisen from the fact that water vapour absorbs infra-red radiation (59). In the method published by Johnson and Shuster (60) infra-red radiation from two sources passed through two conductor tubes, and then into two chambers of a detector. One gas stream was dry, but the other gas stream came from a collection chamber attached to the skin and so consequently contained water. In this detection chamber radiation was absorbed by the moisture and gave rise to an imbalance between the two sides of the detector; the imbalance was measured electrically, amplified and displayed on the calibrated meter of the analyser, which in turn was connected to a recorder. There is a linear relationship between the area under the calibration curve and the volume of water analysed, this area being dependent on the flow rate of dry gas.

Direct recording of axillary ratio

James (28) recorded the axillary ratio itself, rather than its components, by using an x-y recorder. Perspiration from each axilla was collected by gas

streams passing through chambers attached to the axillary skin. The moist gas streams passed into two separate moisture meters where electrolytic decomposition of the water converted phosphoric acid into non-conducting phosphorus pentoxide and the instruments indicated the changes in conductivity. The electrical signals representing changing moisture levels in each axilla were then passed to an x-y recorder, which plotted the two values and provided a trace of the axillary ratio. Retraces were run for 15-30 min and from them an accurate slope for the ratio of sweat in each axilla was obtained.

Factors affecting sweating

A wide variety of factors influence sweating and, if meaningful sweat studies are to be undertaken these factors must be eliminated, or allowed for, in the test procedure adopted. Some of the more important factors are:

(i) A high relative humidity promotes over-production of sweat (unless air movement is high) because impaired cooling of the body surface allows the internal temperature to rise (29); this is made use of to aid promotion of sweating in experimental studies.

(ii) A variable time is required for an equilibrium sweating rate to be attained; in some subjects several hours may be necessary (29). Measurements should not be made until the subject has been allowed time to equilibrate with his surroundings.

(iii) Emotional or mental stimulation causes a rapid onset of sweating; in thermal studies this may constitute an uncontrolled variable (29).

(iv) The position of the trunk during sweat collection affects sweat production in various parts of the body, including the axillae. Localized unilateral pressure will cause a reduction in sweating on the part of the body where it is applied and a corresponding rise elsewhere (29). This effect may occur if a bulky collection device is used in the axilla, or if the subject sits sideways in his chair.

(v) If a subject falls asleep during the period of a test, perspiration may become quite erratic (28).

(vi) Variations in sweat production are observable in different skin areas corresponding to variations in the numbers of glands on different parts of the body (61). Comparative assessments of materials must always be carried out on equivalent skin areas.

(vii) Skin temperature has a definite localized influence on sweating; a high local temperature leads to an increase in sweat output. Skin temper-

atures over 33°C show this effect (62). Techniques involving air flowing over the skin must not cause local cooling, which will have the converse effect of reducing sweat secretion.

(viii) Under different conditions the same stimulus may elicit differing sweat gland responses; this is referred to as 'conditioning' of the eccrine sweat gland (10). Environmental temperature is a 'conditioner'; sweating induced by a heated, artificial environment, or by drugs is less pronounced in winter than in summer (61).

(ix) There may be sex differences in the period required for sweat to appear on the skin surface following stimulation of the glands, although in the axilla similar amounts of sweat are found in both sexes (63). The period in females is longer than in males, and the proportion of males and females must be equal in different treatment groups.

(x) Metabolic rate, which is influenced by exercise, thyroid function, fever, intake of food, etc., affects the quantity of sweat produced (29). If tests are being carried out on a number of subjects over several weeks, it is always desirable to make collections at the same time of day on any one subject. Subjects receiving hormone therapy should be excluded from the tests.

Antiperspirant materials

Until the introduction of an aluminium chlorhydrate complex (13), the most popular antiperspirant materials were aluminium sulphate and aluminium chloride. Since its introduction aluminium chlorhydrate has been, and still is, widely used. In aqueous solution the aluminium salts usually are acid, and this may prove irritant to skin and is certainly damaging to textiles in contact with them. Aluminium chlorhydrate yields a less acidic solution than the other aluminium salts.

Formalin is an effective anhidrotic (used mostly on the feet), but owing to its presence in crease-resistant fabrics many people are becoming sensitised to it (11).

Zirconium salts (11, 36) have not been in general use as antiperspirants since 1956 when it was discovered that they may lead to granuloma in the axillae; this was considered to be an allergic reaction which could be potentiated by the use of soap and hexachlorophene (11).

In 1969, Alphin, Vocac, Saunders and Ward (18) reported the results of tests, carried out on cats, to assess the effect of lignosulfonates on pilocarpine-induced sweating. Two of the materials tested produced a signi-

ficant reduction in sweating and in the case of one of them the reduction was comparable to that obtained with aluminium chlorhydrate. Preliminary tests indicated a reduction in emotionally-induced finger sweating.

Some of the more interesting materials for consideration as possible antiperspirant ingredients are anticholinergic drugs, which are parasympathetic blocking agents (64). Impulses carried by the parasympathetic system stimulate eccrine sweat secretion; under parasympathetic stimulation, acetylcholine is formed at the peripheral nerve endings and serves as the chemical mediator transferring impulses to the receptor cell in the secretory region of the gland. Acetylcholine is rapidly broken down when excitation of the nerve ceases. An anticholinergic agent does not block formation of acetylcholine but in some way prevents the receptor cell responding to it, so theoretically anticholinergic agents can be utilized to suppress sweating. Unfortunately both natural and many synthetic anticholinergics are not very selective in their action and unpleasant side-effects (dryness of the eyes and mouth, headache, blurring of vision, dizziness, hesitancy of micturition) may occur. Although many of the side-effects are reduced if the administration is topical rather than by injection, because the ability of these compounds to penetrate skin is poor, for the same reason their effects on sweating may be less than that obtained with aluminium chlorhydrate. Iontophoresis of the drugs would promote absorption, but is of limited practical value as it requires medical supervision.

MacMillan *et al* (26) found that esters containing one or more elements of the atropine or scopolamine structure were most effective in reducing perspiration and effectiveness was related to skin penetration in the case of the esters of scopolamine hydrobromide. A 0.025% solution of the benzoyl ester of scopolamine could be applied repeatedly to a limited area of the body without any evident systemic effects; the authors estimated that the whole body surface would have to be covered more than once to promote even minimal systemic effects. This solution gave a 35% reduction in axillary sweating.

Reductions in sweating of 40-68% were obtained by repeated daily applications of 0.5% solutions of hexopyrronium bromide (25), and it was calculated that subjects used about 15 ml of this solution per week. Used on the abdomen, under occlusion, a 1.0% solution of hexopyrronium bromide gave complete inactivation of sweating for a period of 2-3 days, but three out of fifty subjects experienced side-effects (53).

A 4% solution of poldine methosulphate (*Nacton*) caused complete

suppression for 2-3 days on the forearm, but was less effective in water than in alcohol (54). Possibly because of lack of penetration, poldine methosulphate was less effective on the palms, soles and axillae than on other areas of the limbs and trunk.

Studies on the foot-pad of mouse and rat (21) using two anticholinergics *Priamide* (1.0% and 2.5% in alcohol), and *BRL 556* (1.0%, 3.0% and 10% in alcohol) showed an inhibiting effect, the duration of which depended on the concentration and amount applied. Although applications were made on one foot only, the inhibiting effect was frequently seen in the other foot pad also.

The importance of the vehicle on the efficacy of an antiperspirant has been shown by Kligman (65, 66) who used dimethyl sulfoxide (DMSO) to aid penetration of aluminium salts. Although this particular vehicle is not suitable for inclusion in cosmetic products because of its toxicity, other less toxic vehicles which show a potentiating effect may be available and should be considered when the antiperspirant product is formulated.

Mechanism of the effect of antiperspirants

The mechanism by which antiperspirants exert their effect is not completely clear.

With regard to aluminium salts one suggestion (11) was that they cause narrowing of the sweat duct by protein precipitation and enhanced keratinization. Another suggestion (4) was that the secretory portion of the duct carried a negative charge which attracted the biologically electro-positively charged aluminium salts, thus inhibiting sweating.

Penetration studies of aluminium salts (67) using radio-tracer techniques, suggested that following topical application insufficient aluminium reached the dermis to exert a physiological effect on the gland.

Papa (68), and Papa and Kligman (69) described experiments in which *Sellotape* stripping, methylene blue iontophoresis and histological examination were carried out to determine the action of the anhidrosis brought about by water, formalin, and aluminium salts. From their results they suggested that the temporary anhidrosis caused by water is due to swelling of the horny cells near the eccrine duct orifice which causes closure of the pore. With formalin a plug of material is formed in the duct due to protein precipitation. In the case of aluminium salts the authors postulated that there is an alteration in the permeability of the epidermal portion of the duct and although the gland functions normally, the sweat leaks out into

the surrounding tissue before it has a chance to reach the skin surface. They likened the sweat duct after treatment with an aluminium salt to a 'leaking hose'.

Conclusions

There are a variety of methods for assessing sweat gland activity at the disposal of the cosmetic manufacturer. In considering which method to adopt as a routine test for assessment of the antiperspirant effect of topically applied materials, several factors must be considered. The choice will be influenced by the effect to be measured: complete inhibition of sweating, or only partial inhibition requiring measurement of small differences in the effects of products. Almost as important is the ease with which the method can be carried out and its acceptability to personnel participating in the trials. From this latter point of view colorimetric techniques are not ideal and many instrumental methods, if used for measurements in the axillae, require the arms to be in a raised, fixed position for long periods. Although these instrumental methods offer the most accurate means of monitoring perspiration, a well-designed collection chamber which fits comfortably into the axilla is necessary before such methods can be adopted as routine procedures for axillary studies. Until such a chamber is available the gravimetric 'pad' method will probably continue to be widely used.

The environment in which the studies are carried out must promote sweating, but must as far as possible exclude any factors which adversely affect the production of sweat, for example, emotional influences or application of local pressure.

At the present time there appears to be no antiperspirant material which is any more effective than aluminium chlorhydrate whilst possessing the safety-in-use characteristics of this compound.

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DISCUSSION

DR. D. JACKSON: The cyclic appearance from the chart over the first half hour collection is very striking. Did the output of sweat fall to zero between the peak events?

THE LECTURER: Initially, when stimulating the glands, particularly by heat, there is periodic activity of the gland. At first only a certain number react and there is a return to zero between peaks of activity. Then as the stimulus is maintained, more glands begin to react, each with a greater output, so that ultimately there is a continuous output rather than just periodic activity.

DR. D. JACKSON: Do you have any estimate of the sweat output in these conditions?

THE LECTURER: In a 10-min collection period, a subject sweating heavily would yield perhaps as much as 3 or 4 g of liquid per axilla.

MR. D. ANDREWS: Although you use a panel of subjects for these evaluation tests, if one subject was treated several times over a period of weeks, would you get effective reproducibility?

THE LECTURER: Under the same conditions, if the subject was treated with the same material, fairly reproducible results would be obtained. The traces suggested this. On the other hand, the material with which the subject is actually treated will have a marked effect on the glands and the effect is obviously liable to change over a long period of treatment.

MR. W. D. ROBERTSON: Does this method lead to a simple figure of percent reduction for an antiperspirant compound?

THE LECTURER: With traces of this type, although the results could be treated mathematically it may well be preferable to avoid this type of calculation. For such a calculation, it would be necessary to sum peak heights on the trace to provide quantitative data. Alternatively, it would be possible to select a certain point on the trace for measurement and subsequent calculation. Methods of treating these results are still under consideration, but the final approach may be similar to that used in gas chromatography; namely, measurement of the area under the trace.

DR. D. W. G. DICKER: Have you been able to correlate your results with the perception of antiperspirant activity obtained with home-use conditions?

THE LECTURER: No. Our experience with the pad method shows that often the results obtained under experimental conditions do not correlate closely with the results from home-user tests. At home, the person often removes much of the material by getting dressed almost immediately after application of antiperspirant. Also, soap remaining on the skin after washing may interfere with the action of the antiperspirant. Hence the results obtained under experimental conditions are often quite different from the results of home-use.

MR. M. K. SHEPHERD: You conducted your experiments over 70 min in the warm-room. How long would the activity of this antiperspirant actually last?

THE LECTURER: Most cosmetic manufacturers hope that their antiperspirants last over several hours. Under conditions in the warm-room it is difficult to say how long the effect lasts. It is quite possible that under conditions where there is very heavy

sweat output, say the last 25 min in the warm-room, much of the antiperspirant is being washed off the skin. On the other hand, if the antiperspirant is an aluminium salt, the suggested mechanism is that it alters the physiology of the duct to some extent, so that there is leakage of sweat into the axillary skin around the sweat outlet. In warm-room studies the antiperspirant has already made this alteration to the sweat duct when the measurements are being made. If this is the mechanism the effect, presumably, should last quite a considerable time, even if residual antiperspirant is washed from the skin surface.

MR. M. K. SHEPHERD: Normally, roll-on deodorants are supposed to last longer than the dry antiperspirants. Was this so in your experiments?

THE LECTURER: I have no experience of dry antiperspirants. Under experimental conditions we are making measurements within 2-3 h of the time of application of the antiperspirants.

DR. D. JACKSON: You have mentioned that stimulation of eccrine glands can be achieved by iontophoresis of pilocarpine. I wonder if you have any evidence suggesting an adrenergic mechanism of sweat control or production. One group of workers who have used iontophoresis compared nor-adrenaline plus pilocarpine with pilocarpine alone. In the former case there was a significant increase in concentrations of sodium chloride in sweat and they suggested that this type of mechanism may also be involved as well as the cholinergic ones. Have you any comments to make on this possibility?

THE LECTURER: Are you suggesting that one should control sweat by using an anticholinergic agent?

DR. D. JACKSON: Not directly. I wondered if you found any evidence to suggest an adrenergic method of sweat control in addition to the cholinergic one.

THE LECTURER: We have done no work on this aspect: this paper is a review of the methods that are available for antiperspirant evaluation. Our own methods and the materials we have studied are purely the commonly available ones, such as aluminium salts. It is possible that eccrine sweat glands have dual innervation with cholinergic and adrenergic nerves supplying them, but we have not investigated this.

MR. N. J. VAN ABBÉ: The literature seems to be more firm in suggesting adrenergic innervation of the apocrine glands rather than the eccrine glands. I think it would be generally accepted that the eccrine glands primarily concerned with sweat are cholinergic, but there is some doubt about the apocrine.

DR. D. JACKSON: Yes, this is relatively new information. I think the authors were pointing out that eccrine glands were previously thought to be cholinergic in the main, but their recent evidence seems to suggest that adrenergic mechanisms may also be involved in the control of these glands.

MR. N. J. VAN ABBÉ: I think it is well established that an anti-cholinergic drug will give 100% inhibition of eccrine sweat for several days. But the *axillary* eccrine glands are not as much affected as glands in other parts of the body. I have not seen an explanation for this difference.

PROF. F. J. EBLING: I do not know why this should be, but I should like to add the

comment that maybe there is more than one type of eccrine gland. It seems pertinent to me that a high proportion of mammals have eccrine foot-pad glands. On the other hand, eccrine glands are seldom present in hairy skin. It seems to me a surprising fact that the eccrine glands on the hand and foot develop much sooner in the foetus than the others, and I suspect that there are at least two phylogenetically and physiologically different types of eccrine glands and perhaps even more.

DR. D. JACKSON: The workers to whom I previously referred, have suggested this delineation of two types of eccrine gland and have suggested that possibly the adrenergic mechanism may be responsible for producing different types of sweat in the glands of the palms and the soles compared with the eccrine glands in other parts of the body.