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A Comparison of the Effectiveness of Several External Antiperspirants

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Synopsis—The **anhidrotic effects of aqueous solutions of formaldehyde, aluminium chloride, zinc chloride, hexamethylene tetramine, and sodium hexametaphosphate** were investigated on the **volar side** of the **forearm of human subjects. Changes** in the **dynamics** and **quantity of sweat** were recorded with a quickly responding **resistance hygrometer** (< 0.5 sec.) and simultaneously with a **contact indicator test** under conditions of **physiological sweating caused by heating.** Changes which occurred in the **microstructure of the epidermal surface** were objectively examined by the **contact print method** according to Sarkany and Caron. Based on the rate and the intensity of the anhidrotic effect, formaldehyde appears to be most effective; it is followed by aluminum chloride and finally by zinc chloride. The **renewal of sweating after successive stripping** indicates that the anhidrotic effects of the above agents is related to the **mechanical closure of the eccrine sweat ducts** as a result of **denaturation-caused contraction of the horny layer.** The depth of the contraction changes depending on the concentration and the period of application of the tested anhidrotic agent. The antiperspirant action of hexamethylene tetramine could not be demonstrated on the forearm due to the absence of sweat which is essential for the release of formaldehyde. Sodium hexametaphosphate does not reduce sweating; it appears to act by accelerating the hydration of the horny layer and thus facilitating speedier and more intensive penetration of other antiperspirants. The need for considering the physiology of sweating and the characteristics of the epidermal surface in the experimental evaluation of the antiperspirant effects of anhidrotics has been stressed. This includes differences between various body areas, temperature conditions of the examined person, etc. **Non-occlusive moistening** of the control area with distilled water leads, depending on the time of exposure, to an **increase in sweat output** and to **changes in the imbibition of the expelled sweat into the periporal horny layer.**

Sweating has fundamental significance in the maintenance of the proper levels of water and temperature of the body as well as in the hydration and "plasticization" of the surface horny layer (1) (2) (3). Deliberate regulation of the intensity of generalized sweating and of sweating limited to certain areas of the body is often expedient not only for clinical and therapeutic reasons but also for social and cosmetic considerations.

The intensity of generalized sweating can be influenced by a number of

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physiological factors or by artificial means (cooling, heating, relative humidity of the air, drugs, etc.). The intensity of local sweating can be increased in specific limited areas by several locally applied drugs; however, this is of significance primarily for experimental work.

Topical agents, capable of limiting or temporarily stopping excessive sweating on a given area of the body surface, have found much greater utility in medicine and cosmetics. In addition to the other effects, their application leads to changes in the microcirculation of water in the skin and can form the etiopathogenetic basis for certain pathological skin conditions, such as miliaria etc. The objective evaluation of the antiperspirant effects of various agents used for this purpose is very difficult; and in such studies, several basic physiological facts related to sweating must be considered.

On the palms and soles, the regions of so-called psychic sweating, the structural and chemical dissimilarity of the thick horny layer (2), the position of the person under study (3) (4), and the intensity of the psychic or sensory stimulus (5) are significant. In these areas, penetration of externally applied drugs occurs primarily through numerous eccrine sweat ducts of glands which are continuously elaborating sweat.

In the extra-palmoplantar regions, the areas of so-called thermal sweating, sweating can be caused by the generalized or local application of drugs, such as pilocarpine, or by general heating. Pharmacological sweating differs from physiological/thermal sweating both in the course and the composition of the expelled perspiration (6). Absorption in these areas occurs primarily via the direct transcorneal path and to a lesser extent via the hair follicles. Absorption via sweat gland ducts does not occur under normal temperature conditions. In the evaluation of experimental data one must realize, however, that even under subthreshold thermal stimulation, psychic sweating may occur in extra-palmoplantar regions in the same way as on the palms and soles (5).

The penetration of antiperspirants and also the depth of their action are largely dependent on the degree of hydration of the surface horny layer which in turn is significantly influenced by the type of vehicle from which the antiperspirant is applied (7) (8) (9). Excessive hydration, i. e., conditions of occlusion, can by itself limit sweat output through swelling of the terminal portions of the eccrine sweat duct (hidromeiosis) (10) (11) (12).

The authors have attempted to overcome the noted difficulties via a rational approach based on current publications. In addition, the authors' experience was utilized which was obtained during earlier work in this field (a combination of the measurement of the actual sweat output with the aid of a quickly responding resistance hygrometer and of a perspiration print test with the aid of a contact indicator). Simultaneous application of these methods yielded a complete picture of the quantity and the dynamics of sweat secretion and of the frequency distribution of active sweat glands. This type of information cannot be obtained simply by employing only one of the two above-mentioned methods. During recent years many authors have dealt with problems associated with the evaluation of topical antiperspirants [(13) to (25)].

The antiperspirant efficacies of several chemical agents, which are used either in pure form or in combinations for topical antiperspirancy as well as deodorization, are compared in the present study. It includes formaldehyde, aluminum chloride, zinc chloride, hexamethylene tetramine, and sodium hexametaphosphate.

Materials and Methods

The anhidrotic effects of aqueous solutions of the following chemical agents at the indicated concentrations were investigated:

Formaldehyde—1%, 5%, 10%; aluminum chloride—15%; zinc chloride—5%; hexamethylene tetramine—20%; sodium hexametaphosphate—10%.

For control purposes, distilled water was tested by the same procedure. The exposure to the test agent was either 1, 3, or 10 hours. Measurements were commenced within one hour after the removal of the test material from the volar side of the forearm.

Method of Application

Several layers of Whatman 1 filter paper squares (4 $\times$ 4 cm) were moistened with the test solution of the antiperspirant and applied to a previously delineated area. The central portion of the moistened squares was then covered with a polypropylene film to an extent of approximately 2 $\times$ 2 cm. The purpose of this partial covering with a water-proof film was twofold: to prevent rapid drying of the test solutions; and to allow partial evaporation of water vapor formed underneath the occlusive film. The occurrence of anhydrosis due to excessive swelling of the horny layer (hydromeiosis) was thus avoided; and the efficacy of this procedure had been verified by preliminary experimentation. It was also possible to remoisten the protruding filter paper margins with the solutions of the tested antiperspirants whenever long exposures were required. The final fixation to the skin was carried out with a layer of polyurethane foam sponge and a bandage. Tests were conducted on a total of 15 subjects ranging in age from 14 to 16 years. Sweating was elicited by exposing the subjects to heat in a polypropylene tent with the aid of a hot air stream (55 °C). During the measurement, the test subjects were lying in a supine position on a soft polyurethane foam sponge (molitane®) mat.

The dynamics of sweat output were recorded by a resistance hygrometer with a short response time (< 0.5 sec.) (26). Contact indicator sweat tests, according to Rovenský and Toman (27) were simultaneously conducted and are based on the color reaction between pyrogallol and ferric hydroxide in the presence of water from the sweat.

Microstructural changes in the tested areas on the epidermal surfaces were investigated with the aid of the print method conducted according to Sarkany and Caron (28), and these results have already been published in a separate paper (29). Successive stripping of the horny layer was carried out with the aid of cellophane adhesive tape.

Results

Formaldehyde

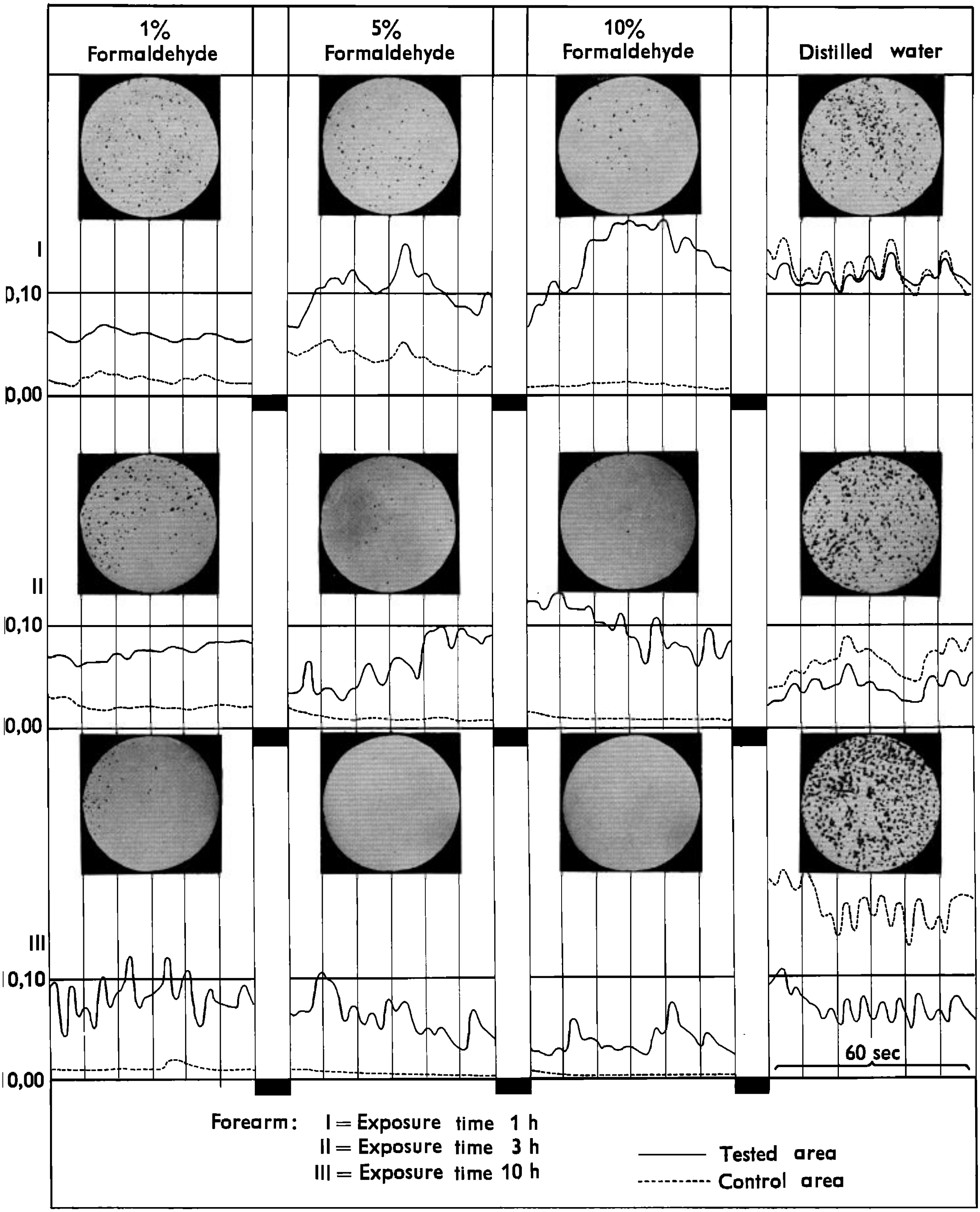
Fig. 1 shows the changes of sweat activity vs. the concentration and exposure time to formaldehyde. By comparing the hygrometric recording of sweat output and the print tests, one clearly notes a growing reduction of sweating in the tested area vs. a simultaneous increase of sweating in the control area as a function of increasing thermal stress. The decrease of sweating is already pronounced in the case of 1% formaldehyde after one hour. This decrease becomes more pronounced with increasing concentrations of formaldehyde and duration of action. Almost complete anhidrosis occurs after the action of 5% formaldehyde for 3 hours, and complete anhidrosis is observed in the case of 5% and 10% formaldehyde after 10 hours of interaction.

The indicator perspiration prints show a decrease of the number and a reduction of the size of the dark spots by comparison to the control area to which only distilled water had been applied. This is a consequence of a constriction and ultimate closure of the eccrine sweat duct caused by formaldehyde denaturation and contraction of the surfacy horny layer. A detail of a perspiration print at a large magnification is shown in *Fig. 5A*.

The hygrometric recordings and perspiration prints in *Fig. 2* and *3* show increasing sweating as a function of the number of adhesive tape strippings at places where formaldehyde had caused either hypo- or even anhidrosis. Both the number and the size of the dark spots on the sweat print are in-

Figure 1

Simultaneous recording of sweating with resistance hygrometer and contact indicator perspiration prints of areas of application of 1%, 5%, and 10% formaldehyde for a period of 1, 3, and 10 hours. Distilled water used as control.



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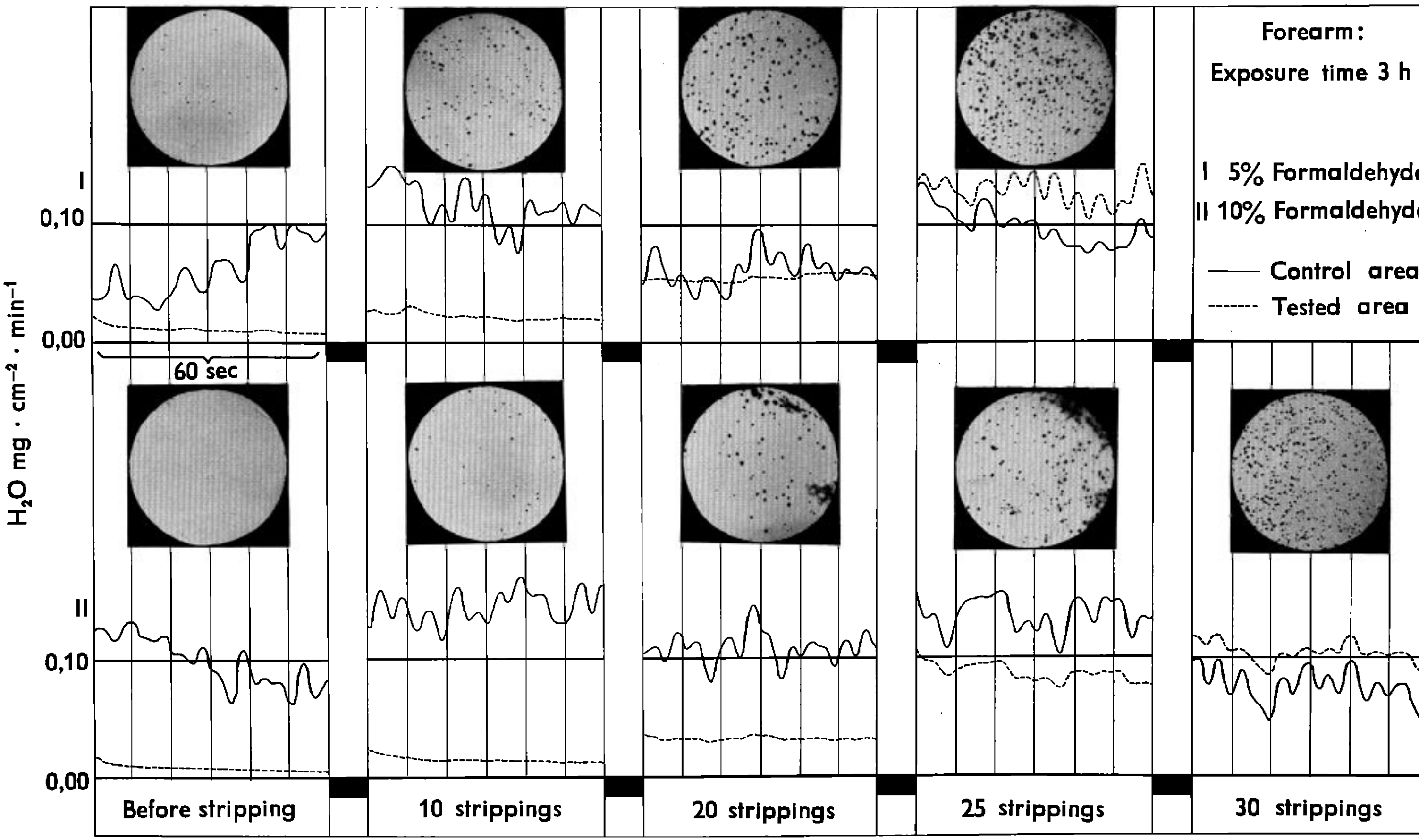

Figure 2

Successive regeneration of sweating of formaline-produced hypo- to anhidrosis as a function of the number of strippings

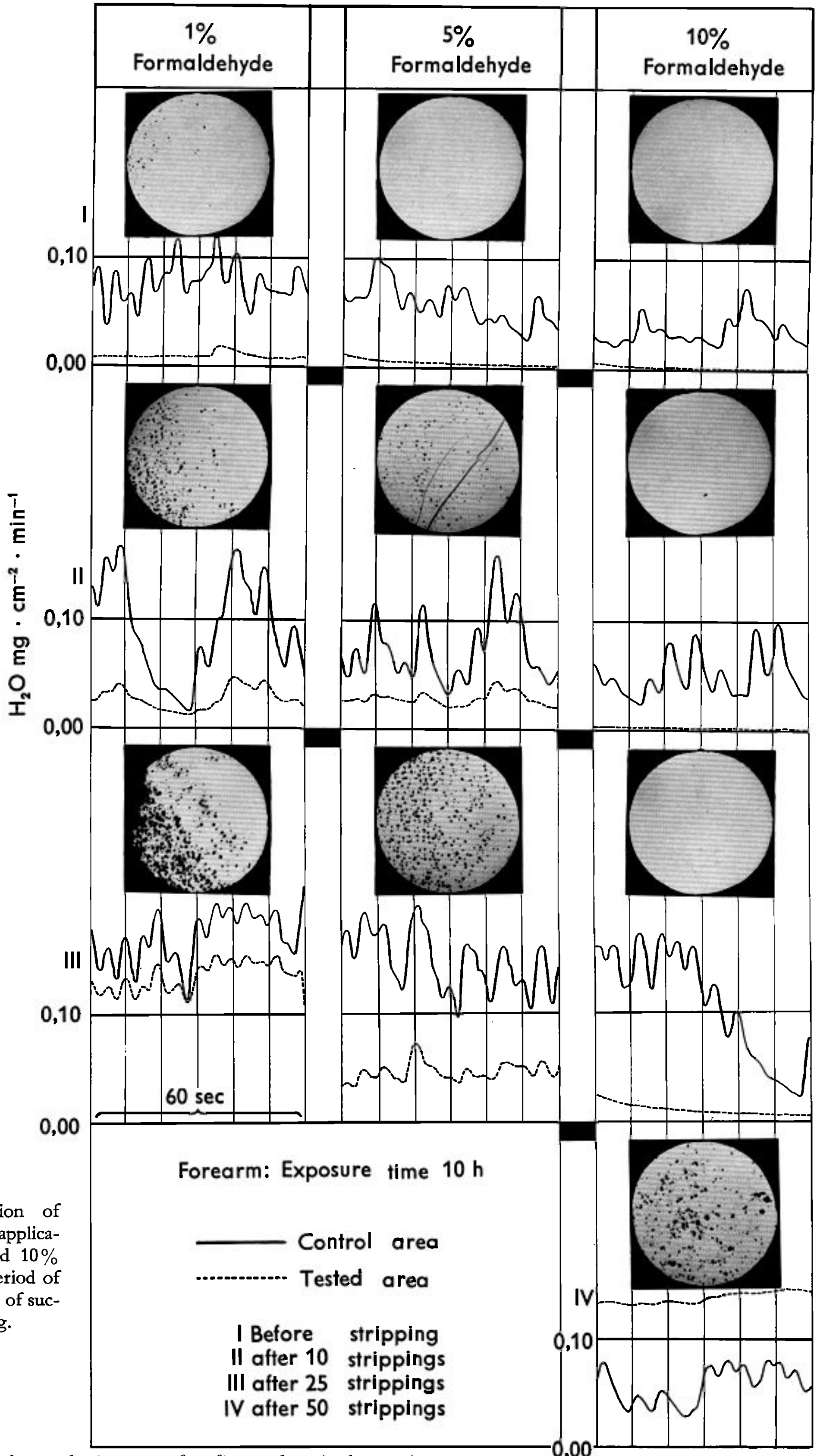

Figure 3

ıccessive regeneration of ṿeating in areas of application of 1%, 5%, and 10% ɪrmaldehyde for a period of ǀ hours as a function of successive stripping.

creased which indicates an opening and widening of the terminal portions of the eccrine sweat ducts which depends on the depth of the formaldehyde denaturation of the horny layer (see also *Fig. 5 C*).

It is interesting to note from *Fig. 3* that, after 10 hours' action by 10% formaldehyde, the barrier is still not severely damaged by as many as 50 strippings which would have become apparent on the contact print by diffuse blackening at the spots at which water had penetrated the barrier.

Changes in sweating after application of other tested materials are documented in *Fig. 4* with the aid of hygrometric recordings and indicator perspiration prints.

Aluminium Chloride

After 3 hours of action, a significant reduction of sweating is observed (see also *Fig. 5 B*) which becomes more pronounced after a 10 hours' application. No complete anhidrosis is observed, however, as in the case of formaldehyde. After 40 strippings, sweat output through the reopened eccrine sweat ducts increases.

Zinc Chloride

After 3 hours of action, the degree of sweating at the tested area is not altered. After 10 hours of interaction, a clear reduction of sweating is noted, but to a much lesser extent than that observed in the case of formaldehyde or aluminium chloride. Forty strippings lead to complete normalization of sweating.

Hexamethylene Tetramine

No influence of sweat activity is observed after either 3 or 10 hours of application on the forearm.

Sodium Hexametaphosphate

This material causes no decrease of sweating. However, after 10 hours of interaction, large polymorphous dark spots appear on the sweat prints which are similar to those occurring after application of distilled water (periporal sweat inhibition).

Distilled Water

As shown in *Figs. 1*, *4*, *5 D*, *E*, and *F*, distilled water is used as a control. Sweat outputs at the same time of interaction is greater than that in a control

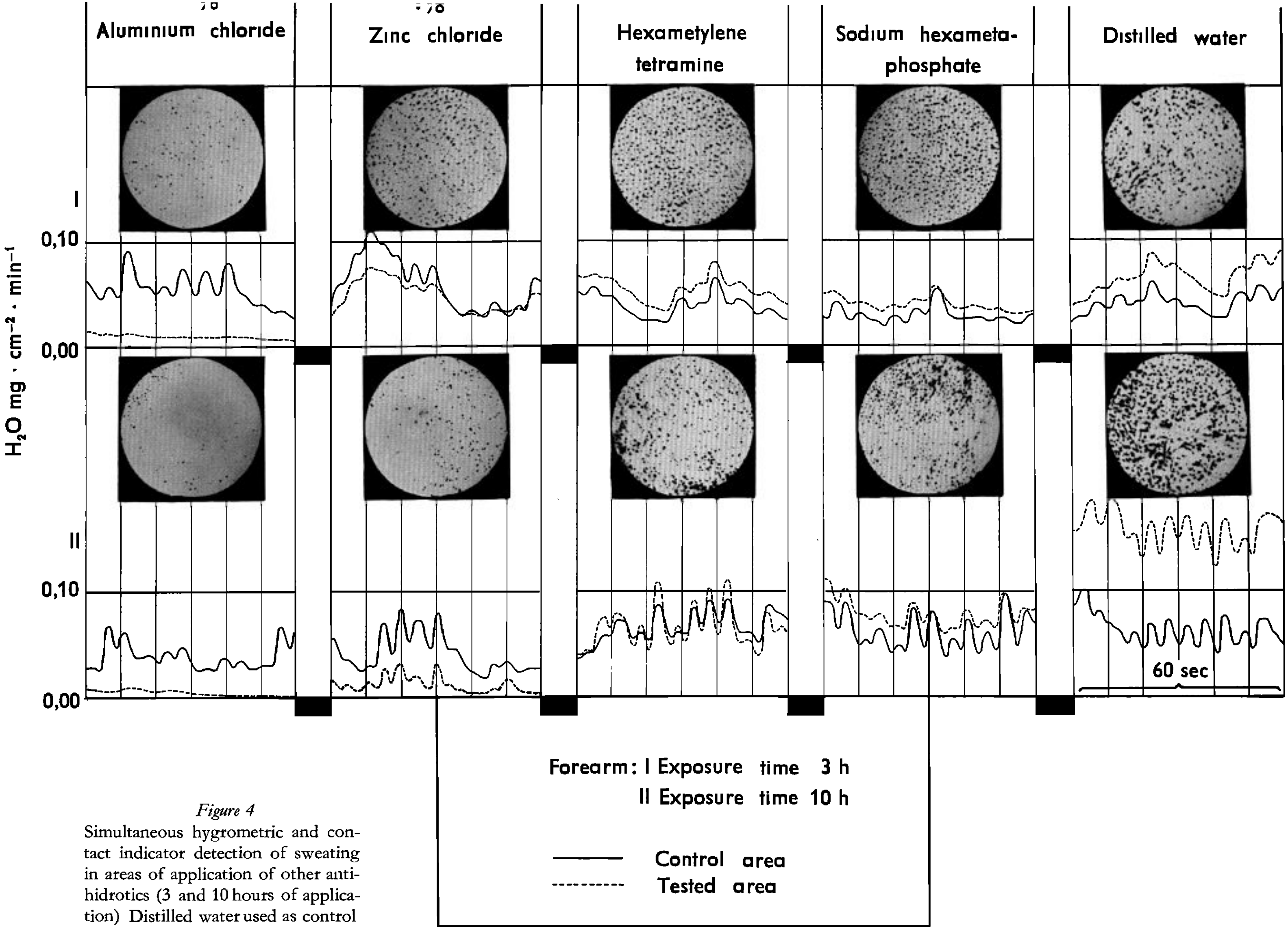

Figure 4

Simultaneous hygrometric and contact indicator detection of sweating in areas of application of other antihidrotics (3 and 10 hours of application) Distilled water used as control

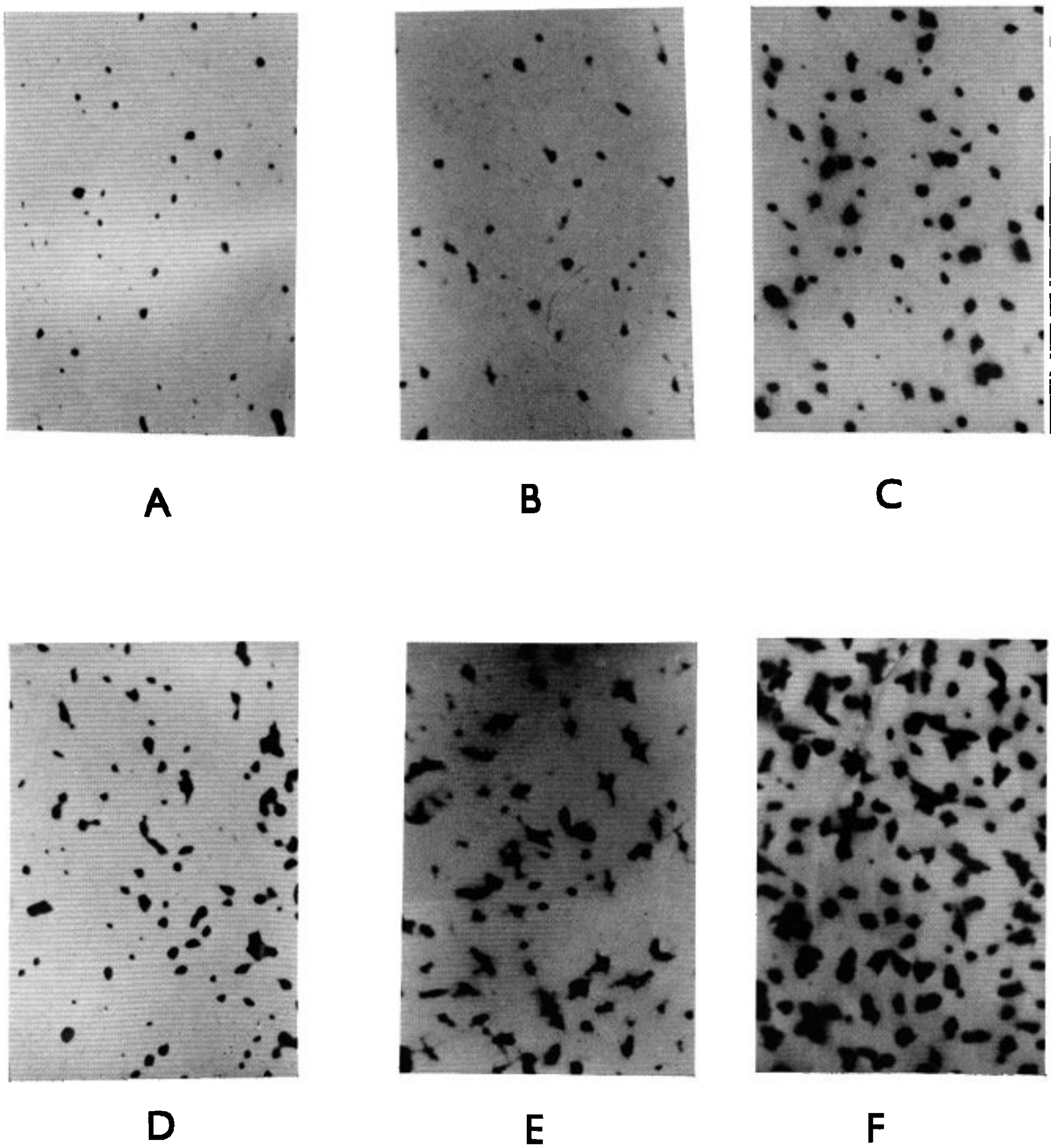

Figure 5

Magnified detail of contact perspiration prints in area of application: A) Formaldehyde 1 %/1 hour—B) Aluminium chloride 15 %/3 hours—C) Formaldehyde 5 %/3 hours; after 25strippings—D) Distilled water/1 hour—E) Distilled water/3 hours—F) Distilled water/10 hours.

(Fortsetzung der Legende auf gegenüberliegender Seite)

of an unmoistened area. On the perspiration prints, one can also see an increase of the large polymorphal spots which are formed by the inhibition of expelled sweat in a periporal relief which is altered by water moistening lasting for varying times.

Discussion

From the above results it follows that, amongst the tested materials, formaldehyde is the most effective anhidrotic even at low concentrations and after short exposure periods. By denaturing the proteins of the horny layer it causes mechanical constriction or even closure of the terminal portion of the eccrine sweat duct (so-called high level blockage) (19) (20). Such microstructural contractive changes of the epidermal surfaces of the palm and the forearm have been verified with the aid of silicone rubber prints by the method of Sarkany and Caron (28) (29). The intensity and depth of denaturation of the epidermal surface are proportional to the concentration of and the exposure time to formaldehyde (3). This is also confirmed by the gradual regeneration of sweating with successive stripping. Denaturation causes modification of the physico-chemical properties of the horny layer and is the cause of varying adhesivity to the stripping tape; as a result, no mechanical failure of the barrier takes place even after a large number of strippings.

Mechanical occlusion of the eccrine sweat duct with simultaneously unreduced activity of the sweat gland effects changes in the water circulation in the skin and leads to dilatation of the eccrine sweat ducts in their epidermal sections (30) (31) (32).

The period, during which sweating is stopped or reduced, depends on the rate of epidermal regeneration as a result of its uninterrupted renewal (horny layer—approximately 6 days, whole epidermis—26 to 30 days) (2).

Explications

to A) Construction to impermeability of most eccrine sweat ducts. Longitudinal elongation of dark spots demonstrates the constriction of eccrine sweat ducts;

to B) Changes after aluminium chloride treatment are the same as those for formaldehyde (longitudinal constriction to closure of a large number of eccrine sweat ducts);

to C) The contours of most detected eccrine sweat ducts are round and wide open which corresponds to their morphological structure in the deeper portions of the horny layer. There is no pronounced imbibition of sweat into the periporal relief;

to D) Polymorphous, mostly isolated minute black spots with marked small dendritical spines;

to E) Larger, polymorphous spots with interconnected spines in the periporal relief;

to F) Intensely black, polymorphous spots, the majority of which is interconnected with the surrounding spots into large merged groups.

The disadvantage of formaldehyde is its well-known sensitization action after repeated application. The authors feel, however, that it should be possible to employ low concentrations (about 1%) in routine use especially with the assumption that this anhidrotic agent is applied repeatedly.

Aluminium Chloride is currently one of the most widely used anhydrotic agents and possesses some advantages over formaldehyde. It has a lower sensitizing potential but is more of a primary irritant due to its acidity in an aqueous medium. There is no unanimity in explaining its antiperspirant action. Denaturation and astringent action which could cause mechanical constriction of the eccrine sweat ducts similar to formaldehyde have been described (20) (21). This concept is confirmed also by recent findings of the authors of this paper. In addition degenerative changes, primarily of the apocrine glands, have been described (22). Recently, Papa and Kligman have carefully studied this complex of problems. They conclude that the antiperspirant influence of aluminium chloride is caused by increased sweat resorption during passage through the eccrine ducts as a consequence of periductal changes due to aluminium chloride (19). Gordon and Maibach conclude that the changes take place below the level of the horny layer (25).

The authors believe that different conclusions can follow from different experimental approaches. For example, the concentration of aluminium chloride is of great importance. The manner and the rate of penetration depend furthermore on the degree of filling of the eccrine sweat ducts by sweat, on the temperature conditions of the subject (sub-treshold thermal excitation and season of the year), and on the period of exposure to the active anhidrotic.

If sweating occurs in the test area, aluminium chloride can conceivably penetrate via the eccrine ducts; thus degenerative changes in the vicinity of the eccrine duct and possibly even in the coiled duct of the sweat gland may occur. Chances for this are especially good in the axillary region, in view of the anatomic course of the eccrine sweat duct and in view of the fact that here, as also on the palm, psychic sweating is almost continuous. One must also take into account the influence of resorption in the axillary region in a manner similar to that under conditions of partial occlusion.

Zinc chloride is employed relatively rarely as an antiperspirant at this time. Its action is that of a slow astringent and the mechanically constricted eccrine sweat ducts can be opened by stripping with adhesive tape.

Hexamethylene tetramine causes no suppression of sweating even after 10 hours of application. The anhidrotic effect of hexamethylene tetramine depends on the liberation of formaldehyde vapors in the presence of acidreacting sweat (17) (23) and can thus occur only in a sufficiently acidic and moist environment which is required for its hydrolysis. Thus, on the volar side of the forearm, where there is no sweating under normal temperature conditions, it exhibits no anhidrotic effect.

Sodium hexametaphosphate and the *metaphosphate polymer* are used as bath additives with antiperspirant action (Calgon®, Dulgon®) (17) (23). From our measurement it is concluded that these materials by themselves have no antiperspirant effect. They act instead as agents which accelerate the penetration of water into the horny layer and thus can assist the penetration of simultaneously or subsequently applied antiperspirants (powders with zinc oxide, boric acid, salicylic acid, etc.). It the bath lasts very long, they can cause temporary constriction or closure of the eccrine sweat duct through swelling of the periporal horny layer.

Distilled water applied to the forearm skin as the control causes, depending on the period of skin moistening, increased sweat expulsion in the test area after a given period of drying. This certainly is not direct stimulation of the sweat gland. On the other hand, one could attribute this effect to hydration (plasticization) of the horny layer which surrounds the sweat gland outlets. The inside dimensions of the outlets regulate the rate of passage of sweat through the eccrine ducts and thereby the quality and the quantity of the expelled sweat and to a degree also the activity of the sweat gland via feedback (33).

Prolonged increased hydration even after termination can lead to changes in the sorptive capacity and sweat diffusion within the periporal horny layer perhaps as a result of the elution of water-binding substances. The authors have shown changes on the epidermal surface after maceration in water by microtopographical prints (29), and these are confirmed by their results from perspiration print tests *(Fig. 5D, E, F)*.

Excessive hydration with total prevention of water evaporation (occlusion) leads, after a period of time, to swelling of the horny layer which includes the periporal rings which can lead to a temporary stoppage of sweating via hidromeiosis. Maceration lasting longer than 48 hours leads to irreversible denaturation changes in the horny layer (34).

Conclusions

From the above results it can be concluded that the tested antiperspirants can be rated with regard to their effectiveness for sweat reduction as follows: Formaldehyde > aluminium chloride > zinc chloride.

Perspiration print tests, microtopographical observations of the epidermal surfaces, and the reversal of hypo- and even anhidrosis by stripping lead to convincing support for a mechanism of antiperspirant action which is based on contraction of the horny layer by denaturation. The intensity and depth of these denaturation-caused changes depend on the concentration and on the time of action of the tested agents. The influence of the hydration of the horny layer on the rate and intensity of penetration of topically applied materials was stressed in the discussion. No anhidrotic effect of hexamethylene tetramine could be demonstrated on the forearm because here, under normal temperature conditions, sweat activity is lacking which is necessary for hydrolysis and liberation of formaldehyde. Sodium hexametaphosphate by itself did not reduce sweating. In the control areas which had been moistened only with distilled water, greater expulsion of sweat was observed after some drying out (1–2 hours); modified imbibition of water in the periporal region was also observed. The discussion also concerned itself with the improved passage through the terminal portions of the eccrine sweat glands as a consequence of hydration (plasticization) of the periporal horny layer. Finally, the possibility of modifying the periporal layer's ability to bind water was explored.

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