Pathways of Ionic Flow through Human Skin *in vivo*

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The pathways of electric current have been examined with special electrodes and methods. The results indicate that the flow through ordinary stratified stratum corneum is negligible, and that the dominant ionic path is through the sweat duct units. Here the cells of interest may be oriented perpendicular to the main stratified orientation of the skin, and this may affect the methods and interpretations of absorption/permeability studies. (Received May 23, 1983.)

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The electric current flow is a measure of the ionic permeability of the skin (1, 2). It is reasonable to believe that the current flows through the sweat duct units. The present paper examines possible other paths of both a.c.- and d.c.-current, and based upon the findings a new model of the morphology of the zones of ionic flow is proposed.

METHOD

An ordinary plate electrode on the skin measures the average value of the skin admittance (conductance and capacitance) under the electrode, a possible nonuniform current distribution will not be revealed. Therefore two special electrodes were used to examine the current distribution. One electrode was a thin wire of diameter 0.15 mm. The usual density of duct pores is 1 to 6 pr mm^2 (3), corresponding to an average distance between pores of 1 to 0.4 mm. The wire is therefore thin enough to distinguish between most of the pores. The other electrode was made of a very thin metal film, so thin that very small currents left current marks in the metal. With both electrodes it was important to avoid lateral conductance along the skin surface. They were therefore used under dry skin condition. Dry skin is defined as the state of the skin when no electrolyte or conductive gel has been applied, after an adequate stabilizing period during which the subject relaxes so that his sweat gland activity has reached a stable minimum and GSR waves are not elicited at non-palmar skin sites (4). The subject was lightly clothed in ordinary room temperature to minimize perspiration.

The following electrodes were used:

(*a*) Metal film electrode. Metal strips about 0.1 μm thick on a glass substrate, width 1.2 mm, length 4–10 mm. The metal is so thin that it is transparent, and it is therefore easy to control both uniform skin contact and the development of the current marks. The electrode was placed directly on dry skin over a length of 4–8 mm, corresponding to a contact area of about 5–10 mm^2.

(*b*) Silver wire, diameter 0.15 mm, electrode area 0.018 mm^2.

(*c*) Pregelled commercial ECG-electrode, Simonsen & Weel, model 888. Around the central sponge with KCl-conductive gel, vaseline was put to prevent gel from spreading out on the skin surface.

(*d*) Reference electrode, flexible metal plate 16×8 cm^2, applied with conductive gel on the same arm as the active electrode.

Skin admittance can be measured by a bridge, but here a lock-in amplifier was used in order to obtain recording facility of admittance variations. 2-electrode measurements were performed with a system giving recorder output of measured conductance G and measured capacitance C_p. Further details including circuit diagram can be found elsewhere (4).

The electric arc was made with the silver wire electrode and either a 5 kV d.c. from a battery-operated megger, or a 6 kHz a.c. from a TV high-voltage transformer. In both cases a 330 MΩ series resistor limited the arc current to about 15 μA.

Palmar/plantar skin has in many respects been found to be different from skin of other sites, and the

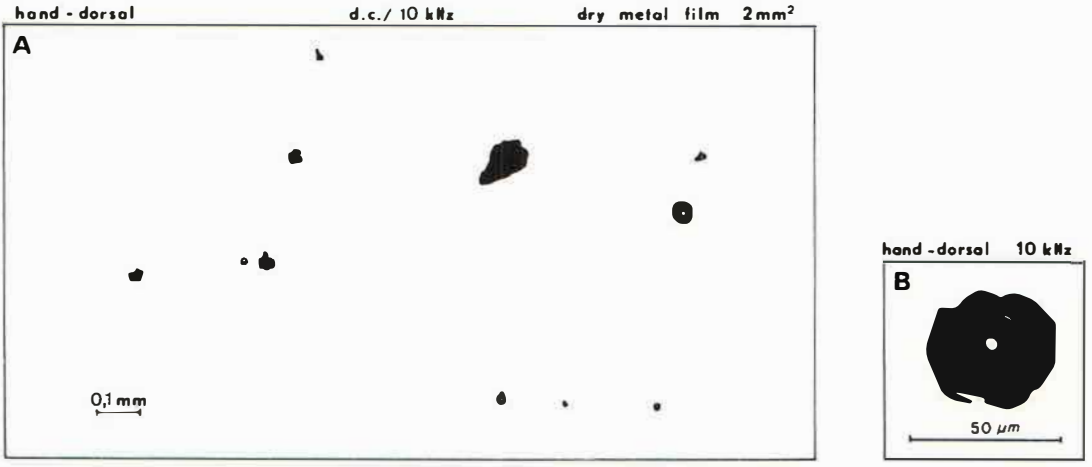

Fig. 1. Current marks on the metal film electrode. (A) Result obtained with a.c. first, then d.c. without change of electrode position. (B) Enlarged a.c.-mark.

validity of the conclusions also for the former is not claimed. All results are typical results obtained with one test subject.

The sweat pores were marked with methylene blue driven into the pores by a positive polarity d.c.-current of about 0.5 mA cm^{-2} for about 100 s.

RESULTS

The metal film electrode was used with a negative d.c.-potential of 30 V, or a 10 kHz 30 V peak a.c. When the electrode was placed on the dry skin of the dorsum of the hand, tiny dots developed after some seconds. The a.c.-current was of the order of 0.5 mA peak, the d.c.-current 0.01–0.02 mA, in both cases increasing. The electrode was removed after about 20 s and examined under the microscope. The current had formed permanent marks in the thin metal. 10 different film electrodes were used on different sites on the dorsum of the hand. The a.c.-marks were different from the d.c.-marks in a typical way. The d.c.-marks were of irregular form and often looked as if a liquid had been splashed out on the metal surface. The size was seldom more than 0.1 mm, and the density 1–2 dots pr mm^2. The a.c.-dots were often more regular and round, perhaps with a hole in the center. Sometimes a circular, scale-like pattern around the hole was revealed (Fig. 1 B). The outer diameter was mostly in the range 0.01–0.05 mm, density about 3–6 dots pr mm^2. Fig. 1 shows a result obtained with both a.c. and d.c. A.C. was first applied, and without changing electrode position the a.c. was disconnected and d.c. connected. Some of the a.c.-dots continued to increase, others did not. A uniform shadow or regular line pattern corresponding to the outlines of the stratum corneum cells, was never observed.

When an electric arc of length about 1 mm was drawn between the silver wire electrode and a metal plate, there were no preferred spots along the surface. When arcs were formed towards the skin, both a.c.- and d.c.-arcs preferred certain skin spots. When no such spots were available, the discharge spread out in a uniform glow over e.g. a square millimeter. Such a glow did not produce a preferred spot even if prolonged for more than 5 s. On a preferred spot a very tiny and clear flash of light often appeared. With negative electrode it could persist, with positive electrode it was always just a scintillation, lasting a fraction of a second. The arc appearance was blurred when a breath was applied towards the spot.

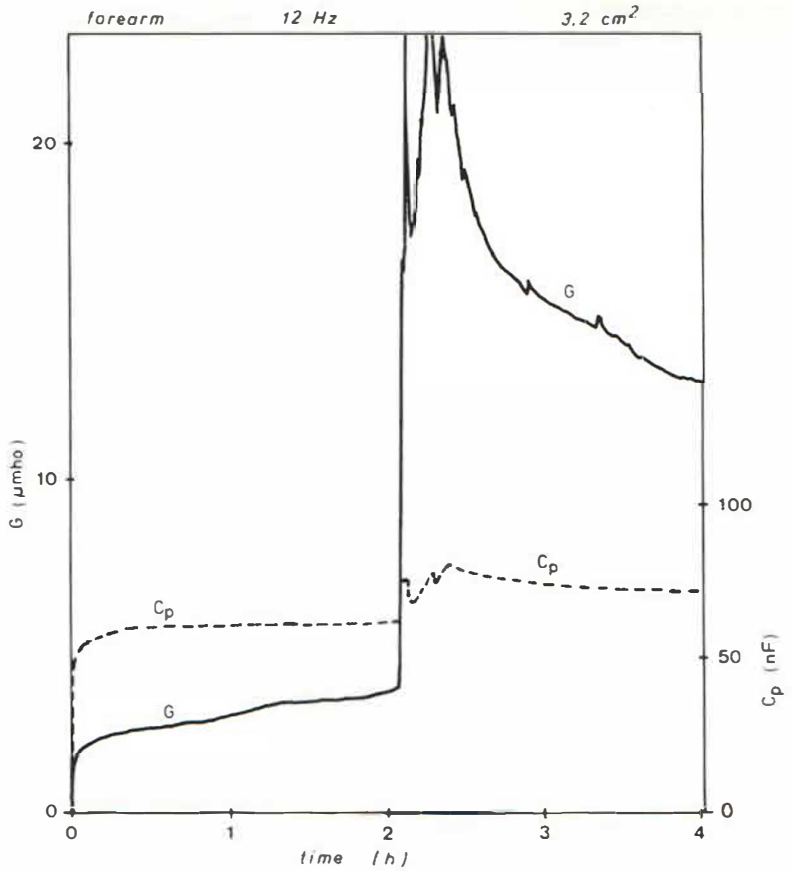

Fig. 2. Trend recording of skin conductance G and skin capacitance C_p, gel electrode.

The preferred spots usually coincided with the marked sweat pores, but not always. A marked pore usually did attract the arc, but not always.

Typical results at 90 Hz with the silver wire electrode directly on dry skin were:

Hand, palmar side	$G = 1$–250 nS
	$C_p = 2$–150 pF
Hand, dorsal side	$G = 0.1$–500 nS
	$C_p = 0.2$–200 pF
Forearm, ventral side	$G = 0.1$–500 nS
	$C_p = 0.2$–200 pF

The smallest capacitance values were not very accurate because of stray capacitance. Also, because of the very small electrode area, electrode polarisation may have interfered. The results therefore do not necessarily represent correct absolute values, but are still useful as relative values to illustrate both the very large spread found, and that there were spots with very low conductance.

Fig. 2 shows the result with the gel electrode. Gel penetration into the skin increased measured conductance G steadily, while skin capacitance C_p was constant. After 2 hours the test subject started a short period of physical activity (knee-bendings). The conductance increased abruptly after a short delay, but the variation in capacitance was small. The

Fig. 3. Rejected model of stratum corneum cells with free ions (dots) in the intercellular space.

large reduction in conductance afterwards indicates that the gel was not able to replace the sweat in the ducts when sweat reabsorption caused the sweat to withdraw.

DISCUSSION AND CONCLUSIONS

Fig. 3 shows a conceivable model of stratum corneum intercellular conductance. The dots are meant to symbolise free ions in the intercellular space.

The result of Fig. 1 together with the electric arc result, demonstrate a strong concentration of both a.c.- and d.c.-conductance into special, narrow skin zones. The results with the thin silver wire confirmed this. Larger areas of uniform current distribution or a pattern corresponding to the cell outlines and intercellular currents there were never registered. Suppose there are liquid films in the intercellular space of the stratum corneum, and that a few molecule-layers have ions which are free to move with bulk liquid mobility. The resistance of an electrolytic film of thickness d, width w and length l is:

$$R = \frac{\varrho}{d}\frac{l}{w} \qquad (1)$$

where ϱ = resistivity of electrolyte.

With $\varrho = 100\ \Omega \cdot cm$, $d = 1$ nm, $l = 30\ \mu m$ (three times stratum corneum thickness) and the dimension of each cell 20 $\mu m \times 20\ \mu m$, we obtain $R = 3\ k\Omega \cdot cm^2$, or 330 $\mu S \cdot cm^{-2}$. Measured skin admittance, Fig. 2, makes it impossible to accept this figure, as earlier also pointed out by Tregear (5).

The conclusion is that the model shown in Fig. 3 must be rejected. Skin current flow is concentrated to special zones of high admittance.

This conclusion is in agreement with Scheuplein (6) who stated that for ions, diffusion through shunt pathways can be very significant. Our results show that also a.c.-currents flow through the same zones. The hole in the center (Fig. 1 B) means that the admittance is not necessarily concentrated to the central part of the duct, on the contrary this may be empty while residual conductive films remain in the annulus zone. Our conclusion is in agreement with the result of Elias et al. (7), that water is stopped by membrane-coating granules filling the intercellular space of the stratum corneum with hydrophobic material. Mere zonula occludens between stratum corneum cells could not stop ionic flow as effectively as found. The lack of complete coincidence between electric arc spots and

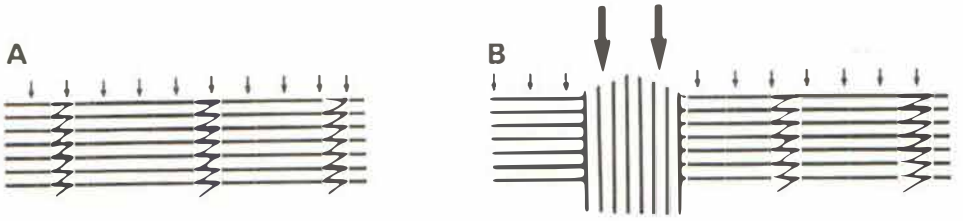

Fig. 4. Models of skin morphology determining permeability. (A) Usual model. (B) Proposed new model of skin ionic permeability.

sweat pore marks may indicate either that not all pores were methylene marked, or that the skin examined had a few other weak spots than the sweat pores.

Fig. 1 showed a large difference between a.c.- and d.c.-current marks. A possible explanation is that d.c. transports water up through the stratum corneum by an electro-osmotic effect (8). At the electrode the water wets the dry metal film in an irregular way.

The ring pattern found with the metal film electrode and a.c., indicates that a.c. flows through the tissue of the sweat duct unit. Earlier results indicate a keratin ring around the duct orifice (9), Abramson et al. (10) showed that the ring was current carrying. It was early shown that the duct has a particular lining of cells (11), and that the outgrowth of the duct is longitudinal from a zone where the duct joins the epidermis (12). It is not surprising that these cells will end *perpendicularly* to the skin surface. The a.c.-pattern shown in Fig. 1 B is in agreement with such orientation, and it is also confirmed by electron-microscopic pictures from non-palmar skin sites (13). The gel result of Fig. 2 indicates that even prolonged contact with a non-aggressive electrolyte did not open the passive part of the stratum corneum, because this would have been accompanied by an increase in measured skin capacitance C_p.

On the basis of our findings, valid for non-palmar/plantar, uninjured skin, we can propose a new picture of the stratum corneum morphology determining skin admittance/ionic permeability. A sketch is shown in Fig. 4.

The proposed morphology influences the interpretation of adhesive tape stripping results (5, 14, 15, 16). According to Fig. 4, the stripping method does not examine the stratum corneum ionic permeability proper, but that of the squamous cells of the sweat duct unit oriented perpendicularly to the skin surface. The viewpoint is changed from a transcellular flow to a flow parallel to the cell surfaces.

The handling of the sweat duct units when in vitro samples are taken, will be important for the in vitro admittance/permeability results. Stratum corneum samples used for biochemical analysis contain only a small percentage of the tissue which determines skin admittance/ionic permeability.

The results obtained with two closely spaced skin surface electrodes (16, 17) will be difficult to interprete. The contribution from skin surface conductance may be dominant, and the contribution from the stratum corneum proper will be difficult to discern from the contribution of the high-admittance zones.

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