Skin Water Loss and Accidental Hypothermia in Psoriasis, Ichthyosis, and Erythroderma

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Accidental hypothermia has been reported in patients with generalized eczema and other erythrodermas, the aetiology of the hypothermia being said to be obscure (Krook, 1960 ; Magnusson, 1960) ; rectal temperatures as low as 83–86° F. (28.3–30° C.) have been described. It has been suggested that hypothermia is related to the increased peripheral blood flow (Mali, 1952 ; Fox *et al.*, 1965). It has also been suggested that the heat loss in erythroderma is due to vaporization of water lost from affected skin, in these conditions the skin water loss being enormously increased (Zoon and Mali, 1957).

Hancock *et al.* (1929) pointed out that there are two kinds of water loss from the skin. The first is from sweating, the second from evaporation of water which has passed by diffusion through the epidermis, the corneous layer and its base behaving as a semipermeable membrane. The water loss by diffusion was designated by Rothman (1954) the transepidermal water loss.

The term " insensible perspiration " has been applied to the skin water loss, which is invisible to the naked eye, the sweat droplets evaporating as soon as they reach the skin surface (Jurgensen, 1924).

Few previous studies of the skin water loss have been done after inhibiting sweating, a satisfactory method for producing complete inhibition of sweating not hitherto being available.

In observations now reported the transepidermal water loss was measured in normal subjects and in patients with erythroderma, psoriasis, and ichthyosis.

Methods and Materials

The transepidermal water loss from normal skin was measured in 40 subjects after sweating had been inhibited with poldine. The apparatus and method have been described in detail previously (Bettley and Grice, 1965).

The apparatus, which estimates the total cutaneous loss from selected areas of the skin, consists of a collecting chamber placed on the abdomen, and dry air is passed over the skin. The amount of water is determined gravimetrically. Sweating is inhibited by the local application of poldine methosulphate (Nacton) (Grice and Bettley, 1966). The area of skin to be tested is marked out, painted with two or three coats of 2% poldine in alcohol, and covered with polyethylene, the edges being sealed. Next day the polyethylene is removed and the abdomen washed with soap and water ; 4 to 24 hours later the transepidermal loss is measured.

The apparatus incorporates a thermistor for measuring skin temperature, and the presence of sweating is ascertained by the galvanic conductivity of the skin. The relative humidity in the collecting chamber was calculated from the measured skin water loss (mg./60 sq. cm./30 min.) contained in the total volume of air passing through the collecting chamber in 30 minutes (ml./30 min.) and the weight of water contained in saturated air at the air temperature in the collecting chamber. This was about 1–2° C. lower than the skin temperature.

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The experiments were performed while the patients were at rest or sleeping, and the room temperature and humidity regulated so that sweating was minimal. The test lasted 30 minutes. During this period the presence of sweating on other parts of the trunk and limbs was ascertained by measuring the galvanic skin resistance and testing by the iodine-starch method (Wada and Takagaki, 1948 ; Wada, 1950).

Ichthyosis.—The transepidermal water loss was measured after inhibiting sweating with 2% poldine under occlusion in nine subjects. Seven had the sex-linked form of ichthyosis and two the autosomal dominant form (Wells, 1966).

Psoriasis and Erythroderma.—The transepidermal water loss was measured in areas of skin affected by localized psoriasis in eight patients and in six cases of erythroderma, five of the latter were psoriatics. In all these cases the skin was painted with 1% poldine and allowed to dry for 30 minutes. No further application was made to the skin. The next day the transepidermal water loss was estimated. In order to avoid irritating the skin polyethylene occlusion and adhesive plaster were not used. In four cases repeated measurements were made at various stages of activity of the disease. In two cases the water loss was measured in areas which had not been treated with poldine and compared with the treated areas. A total of 16 measurements of skin water loss were made in all. Owing to the enormous skin water loss that was found in these cases a slight variation was necessary. In normal subjects, after the transepidermal water loss was measured, no measurable condensation was found to take place in the apparatus. Appreciable condensation on the walls of the apparatus was found, however, to have occurred after measuring the skin water loss in cases of psoriasis and erythroderma. To allow for this the following method was used:

The apparatus was as usual washed out with dry air before starting. The collecting chamber was then placed on the abdomen and straight away the water given off by the skin was collected. A steady state as indicated by the humidity transducer was reached in one to two minutes. As soon as the 30-minute collecting period had come to an end, the collecting chamber was removed from the skin and the air flow turned off. An airtight base was fitted to the collecting chamber and the apparatus reconnected to another water tap. Dry air flow was then passed through the apparatus for 30 minutes, or until no further moisture could be obtained. (The monitoring of the humidity transducer was found to be a useful guide to the rate of drying of the apparatus.) The weight of water thus collected from the apparatus was added to that obtained during the 30-minute skin water loss estimation.

Normal Skin Areas in Eczema and Psoriasis.—After inhibiting sweating with poldine under occlusion the transepidermal water loss was measured in areas of normal skin in patients with eczema and psoriasis.

Results

Normal Transepidermal Water Loss

The water loss by diffusion through normal skin was remarkably small. This was in spite of a very low ambient humidity and free air movement.

The mean transepidermal water loss in 47 normal subjects was 0.35 (S.D. 0.09) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity 2–5%, air speed 23–25 mm./sec.).

No significant correlation was found with age (39 subjects). (Correlation coefficient, −0.22 ; 95% confidence limits for the population correlation coefficient are −0.5 to +0.13.)

The "maximal" possible whole-body daily transepidermal water loss may be estimated from the measured rate of transepidermal loss (mg./sq. cm./24 hr.) and the total surface area (Du Bois formula). The results in 29 patients are seen in Fig. 3. The ambient humidity in the collecting chamber was very dry (2–5% relative humidity) ; the results are therefore higher than would be expected under ordinary room conditions, since the rate of transepidermal water loss decreases with rising ambient humidity. The total actual daily loss will depend on the humidity of the air in direct contact with the skin, which depends on room humidity, the presence of sweating, and the effect of clothing.

The transepidermal water loss also increases with rising skin temperature. The temperatures during the measurements were those of "covered skin," the skin temperature under the collecting chamber being 1–2° C. higher than the adjacent uncovered areas. The transepidermal water loss from the calf and thigh was measured in a few cases, and, though significantly raised, was of the same order as that from the abdomen.

The transepidermal water loss from the calf in five subjects was 0.6 (S.D. 0.12) mg./sq. cm./hr. ($t=4.6$, $P<0.01$). The transepidermal water loss from the thigh in seven subjects was 0.46 (S.D. 0.14) mg./sq. cm./hr. ($t=2.3$, $0.05>P>0.01$).

The mean estimated daily transepidermal water loss in 19 normal subjects was 151 (S.D. 44.2) ml./day, range 63–280 ml./day.

The heat loss by evaporation of 1,000 ml. of water is 580 kilocalories. The daily heat loss from evaporation of the normal maximal transepidermal water loss is therefore 87 (S.D. 25) kcal.

Ichthyosis

The results are set out in Fig. 1. The mean transepidermal water loss was found to be 0.71 (S.D. 0.29) mg./sq. cm./hr. (skin temperature 32–35° C., relative humidity 2–12%). This was highly significantly greater than normal, though in three cases the transepidermal loss was normal ($t=3.9$, $P<0.01$).

On routine testing of sweating from the rest of the trunk and limbs the findings were of some interest. Sweating from the trunk and limbs was strikingly less than normal, while sweating from the areas of "constant emotive sweating" was normal in eight of the nine cases. These areas of emotional sweating are the axillae, face, palms, soles (Kuno, 1956), and over the distal dorsal phalanges and back of the interdigital webs (Grice and Bettley, 1966).

Only one patient had tylosis of the palms and soles (Case 9, Fig. 1), and she had normal palmar and plantar sweating. One patient (Case 6, aged 35) had remarkably little palmar and periungual sweating.

Sweating could not be detected on the trunk and limbs (apart from the emotive areas) in eight of the nine cases (Nos. 1–7 and 9). The room temperature and relative humidity were 20–23.5° C. and 52–66% respectively. The skin temperatures were 34–35° C.

To exclude the possibility that slight sweating was taking place in areas of skin in which sweating could not be detected by the iodine-starch or galvanic skin resistance test, six further measurements of skin water loss were made. Skin untreated with poldine was compared in the same patients with sweat-inhibited areas. The water loss was found to be the same in the two areas. On heating, sweating occurred from the trunk and limbs.

The maximal whole-body daily transepidermal water loss in six subjects was estimated (see Fig. 3). The mean was 348 (S.D. 124) ml./day (skin temperature 32–35° C., relative humidity 2–12%). The maximal daily whole-body transepidermal water loss was therefore about double that of normal subjects. Under ordinary environmental conditions the actual transepidermal water loss will probably be nearer the maximal than in the normal subjects. The reasons for this are, firstly, that in the cases with ichthyosis there was a higher ambient humidity (resulting from the increased skin water loss) in the collecting chamber, and, secondly, under normal conditions, as sweating is depressed in ichthyotics, the ambient humidity over the skin

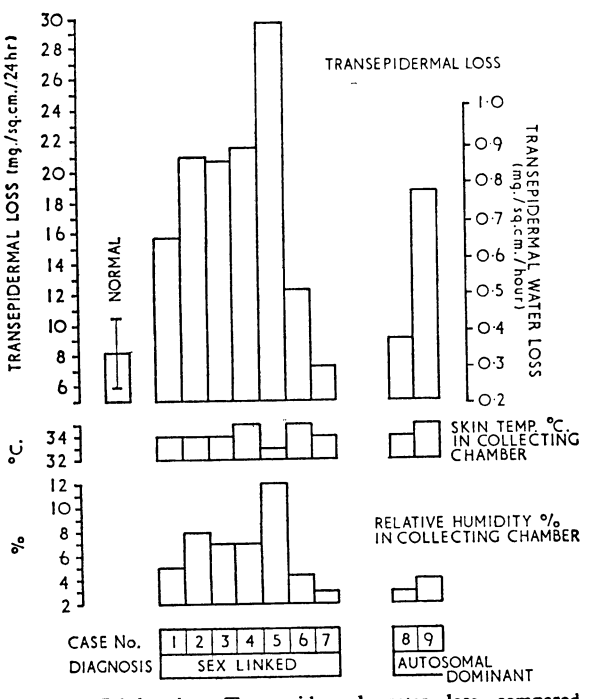

FIG. 1.—Ichthyosis. Transepidermal water loss compared with normal.

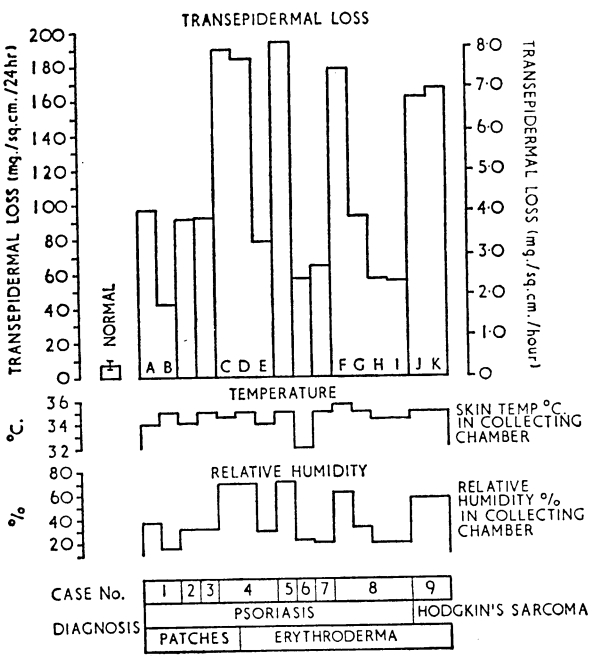

FIG. 2.—Psoriasis and erythroderma. Transepidermal water loss compared with normal. Case 1: B, 7 days after A. Case 4: D, 12 days after C ; E, 22 days after C. Case 8: G, 10 days after F ; H, 12 days after F ; I, 12 days after F, different site from H. Case 9: K, same day, different site, no pretreatment with sweat-depressing agent.

is likely to be less than in a normal person. In normal subjects the relative humidity under a shirt has been shown (Mellanby, 1932) to vary widely between 20 and 70%.

Psoriasis and Erythroderma

The transepidermal water loss in psoriasis and erythroderma was greatly increased. This was in spite of high ambient humidities which resulted from the high skin water loss. The highest ambient humidities were produced in the cases with the greatest skin water loss (see Fig. 2).

The mean transepidermal water loss over patches of psoriasis in eight patients was 5.37 (S.D. 2.6) mg./sq. cm./hr. (skin temperature 34–35° C., relative humidity 10–70%).

When the psoriasis spread and became generalized in one patient with very active pustular lesions (Case 4, Fig. 2) the transepidermal water loss (D) was found to be little changed from the previous measurement over a patch (C). Three weeks later, when the eruption was still generalized but less active, the transepidermal water loss had decreased from 7.7 to 3.2 mg./sq. cm./hr. (Case 4, D and E).

Erythroderma

The mean transepidermal water loss of nine measurements in six cases was 4.96 (S.D. 2.5) mg./sq. cm./hr. (skin temperature 32–35.5° C., relative humidity 20–70%).

The water loss from skin untreated with poldine (Fig. 2, Case 8 I, Case 9 K) was compared in two patients with the transepidermal water loss after sweat inhibition. The water loss can be seen to be similar.

The mean daily whole-body transepidermal water loss in subjects with erythroderma, estimated from six measurements taken at different stages of the disease (see Fig. 3) was 2,158

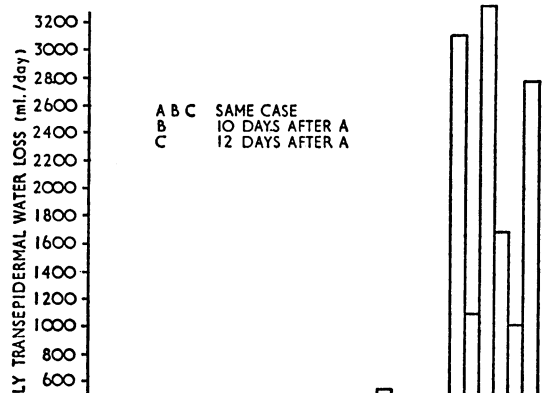

FIG. 3.—Daily transepidermal water loss in normal skin, ichthyosis, and psoriatic erythroderma.

(S.D. 1,019) ml./day (skin temperature 32–36° C., relative humidity 16–72%). The transepidermal water loss is therefore about 10 to 20 times normal.

The ambient humidity in the collecting chamber was very high, the highest water loss resulting in an ambient humidity of as much as 72% (see Fig. 2). Under normal conditions, therefore, the actual daily transepidermal water loss in erythroderma patients may well be nearly as high as that estimated.

The covering of skin with ointments which form an occlusive film will obviously decrease the skin water loss, and under normal conditions there will not be such a free air flow.

The total daily loss of heat from evaporation of this transepidermal water is estimated to be 1,252 (S.D. 591) kcal./day.

Transepidermal Water Loss in Normal Skin Areas in Patients with Eczema and Psoriasis

In 17 cases of eczema the mean transepidermal water loss in unaffected skin areas which had never been affected was 0.55 (S.D. 0.15) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity 5–10%).

The transepidermal water loss is highly significantly greater in areas of normal skin in patients with eczema compared with normal subjects ($t=5.2$, $P<0.01$). The mean transepidermal water loss in unaffected skin areas in 16 cases of psoriasis was 0.41 (S.D. 0.16) mg./sq. cm./hr. (skin temperature 32.5–35° C., relative humidity 5–8%). This was not significantly different from normal ($t=1.8$, $P>0.05$).

Discussion

The present studies show that the loss of water by diffusion through normal skin is remarkably small, 0.35 (S.D. 0.09) mg./sq. cm./hr. This is well known, though in most previous studies of skin water loss sweating was not inhibited. Pinson (1942) found, under conditions similar to those in the present investigation, that the transepidermal water loss was 0.58–1.58 mg./sq. cm./hr. He, however, used the iontophoresis of formalin to inhibit sweating, and iontophoresis may increase the skin permeability (Rothman, 1954). Pinson's results then would be higher than expected. The rate of water diffusion through excised trunk skin is said to be 0.25–0.58 mg./sq. cm./hr. (Mali, 1956 ; Onken and Moyer, 1963).

In spite of a very low ambient humidity, free air flow, and skin temperature similar to that under clothes, the estimated whole-body daily transepidermal water loss was only 151 (S.D. 44.2) ml./day.

A study of skin affected by psoriasis and erythroderma has shown the transepidermal water loss to be enormously increased ; this in spite of very high ambient humidities comparable with those of the clothed skin. This increase of skin water loss, which amounted to over 20 times normal in some cases, was in spite of sweating having been inhibited. A tenfold increase in the skin water loss was reported in psoriasis and exfoliative dermatitis (Felsher and Rothman, 1945), and a sixteenfold increase in burns on the third day (Cohen, 1966). The apparatus used by Felsher and Rothman was a glass collecting chamber in which was suspended a bag filled with calcium chloride.

The daily whole-body transepidermal water loss in erythroderma was estimated to amount to 2,518 (S.D. 1,019) ml./day, being therefore 10 to 20 times normal. The daily insensible skin water loss in erythroderma, measured by weighing patients, was found by Zoon and Mali (1957) to be 1,183 to 2,370 ml./day. This included weight loss from sweating. Sweating is, however, known to be depressed in erythroderma, eczema (Cormia and Kuykendall, 1955), and psoriasis (Suskind, 1954). The total daily skin water loss in erythroderma may therefore well consist largely of the transepidermal water loss.

Complete sweat-duct blockage persisting after heating and methacholine stimulation has been described in erythroderma (Cormia and Kuykendall, 1955) and acute psoriasis (Mitchell and Forstner, 1962). In the present investigation in two of the cases of erythroderma (due to psoriasis and Hodgkin's sarcoma) the skin water loss was found to be the same whether or not sweating had been inhibited.

On the other hand, sweating had been observed in erythroderma during heating (Fox *et al.*, 1965), and in the present investigation palmar sweating was found to be present in

pustular psoriasis after the acute anhidrotic phase of the disease. In the cases where sweat-duct blockage is not complete there may be a partial functional depression of the sweat glands.

It has been suggested that the general state of hydration of the subject might influence the amount of sweat loss (Macpherson, 1960). The large transepidermal water loss with resultant heat loss might equally well influence the amount of sweating in erythroderma.

In normal subjects palmar sweating is constantly present while they are awake (Kuno, 1956); in three patients with erythroderma whose palmar skin was not affected, and had never been affected, palmar sweating we found was greatly depressed.

The increased heat loss, which may amount to 1,252 (S.D. 591) kcal./day from vaporization of the large transepidermal water loss through the skin in erythroderma may also explain the hypothermia which occurs in some of these patients. Mali (1952) showed that there is also increased heat loss from the raised skin temperatures which he found in 83% of the patients with erythroderma. The skin temperatures were about 1° C. higher than normal. In one patient of the present series (Case 4, Fig. 2) with acute pustular psoriasis that was becoming generalized, the skin temperature was 1° C. higher in the affected skin as compared with the adjacent unaffected skin. The heat loss by radiation from 1° C. rise of skin temperature over the whole skin surface is known to be 360 kcal./day (Keele and Neil, 1965).

The raised metabolic rates found in patients with erythroderma (basal metabolic rates +6% to +119%) could be explained by the increased heat loss in these conditions (Mali, 1952). The ^{131}I excretion has been found to be normal (Magnusson, 1960; Fox *et al.*, 1965).

In the present investigation the transepidermal water loss in ichthyosis was found to be approximately double that of normal subjects. In two of these cases there was a history of atopic eczema (Cases 5 and 9), but both patients were free from eczema at the time of testing (for 23 and 40 years). Trunk and limb sweating was found to be depressed, as reported previously (Wells, 1966), but sweating from the palms, soles, and periungual regions was found to be normal in eight of the nine cases. Sweating from the trunk was present during heating, and in warm climates with increased sweating all the patients noticed an improvement of their skin. The comparative sparing of flexures found in ichthyosis vulgaris could perhaps be associated with the diminution of sweat or transepidermal water evaporation at these sites.

Summary

The transepidermal water loss from the skin, due to the passive diffusion of water through the epidermis, was found to be greatly increased in psoriasis and erythroderma, and slightly but highly significantly increased in ichthyosis.

Improvement of the skin condition showed a corresponding decrease in the water loss.

In 47 normal subjects the mean transepidermal water loss from the abdomen was extremely small: 0.35 (S.D. 0.09) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity 2–5%); the maximal loss from the whole body in a dry ambient humidity amounting to only 151 (S.D. 44.2) ml./day.

No significant correlation was found with age. A slight but significant regional variation was observed, the loss from the calf and thigh being greater than from the abdomen.

In patches of psoriasis the transepidermal water loss could be as much as 20 times that of normal, 5.37 (S.D. 2.6) mg./sq. cm./hr. (relative humidity 10–70%).

In ichthyosis the loss was about twice the normal, and sweating from the trunk and limbs was markedly reduced, though sweating from the constantly sweating emotional areas (palms, soles, axillae, dorsal distal phalanges, and face) was normal in eight of the nine cases.

In erythroderma the daily transepidermal water loss was about 14 times normal and could be as high as 2,158 (S.D. 1,019) ml./day.

It is suggested the loss of heat by vaporization of the increased transepidermal water loss could explain the hypothermia and increased basal metabolic rates which occur in some cases of erythroderma.

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