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THE INFLUENCE OF BLOOD FLOW ON TRANSEPIDERMAL WATER LOSS[1]

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Abstract. The influence of blood flow on transepidermal water loss (T.W.L.) has been re-examined and it was found that complete occlusion, venous occlusion and reactive hyperaemia all influence T.W.L. in different ways. Bloodless fields also influence this entity and evidence is presented which indicates that the presence of blood is essential for a normal value of T.W.L. Vasodilation was found either to increase or to decrease T.W.L. Blood flow as such (determined plethysmographically) was found to influence T.W.L. in a non-linear fashion with an increased T.W.L., resulting from a thermoregulatory increase in blood flow to the finger. The results are discussed in relation to the state of present knowledge of the microcirculation in the skin and it is concluded that the precise explanation of the results obtained must await further knowledge of this particular circulation.

The influence of blood flow on transepidermal water loss (T.W.L.) has not been clearly elucidated up to date. Pure arterial hyperaemia, such as is elicited by inhalation of amyl nitrite (11) or by alcohol intake (2), seems in some cases to increase insensible perspiration through the skin, but this was not regularly observed (11, 10). Likewise, T.W.L. was found unchanged or decreased over edematous skin (9), on pitting edema (16) as well as over histamine wheals (12, 13, 15). Newburg & Johnston (14) found that vasodilation produced an increase, and vasoconstriction a decrease in insensible perspiration. Hardy & Söderström (5) previously found that these changes could not be obtained at a skin temperature below 28°C, and in 1942 Pinson (15) reported that no effect could be shown after inhibition of the sweat glands. In 1967 Grice (4) found no changes in T.W.L. with changes in the vascular state of the skin.

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Contradictory and inconsistent results have, thus, been obtained with these investigations and most workers measured insensible perspiration and not T.W.L. The work reported here is the result of a reinvestigation of this problem and evidence is presented that blood flow does indeed have a profound influence on the transepidermal component of insensible perspiration.

MATERIALS AND METHODS

The capsule used in this investigation is a modification of an unventilated capsule, in that the enclosed volume of air is circulated by means of a motor-driven fan. The apparatus has been described in detail elsewhere (8) and briefly it consists of a capsule covering an area of 8 cm^2. The fan is built into the side of the capsule and the speed of rotation is controlled to an arbitrarily chosen level. The absorbant material used was Anhydrone (dried magnesium-perchlorate) which was introduced into the measuring capsule by means of containers which could be screwed airtight into the capsule. The containers were transported in airtight capsules which were weighed before and after a T.W.L. determination. It should be mentioned that high values of T.W.L. are recorded with this method and that the usual methods of determining T.W.L. probably result in a "dehydration" of the skin due to the fact that too lengthy measuring times are employed. (If T.W.L. is measured successively for 3 min periods the value steadily decreases to a constant value after 20–23 min.) These results have been fully discussed elsewhere (7). In this investigation a measuring time of 3 min was used and all values reduced to a standard of mg/5 cm^2/3 min.

The experiments were all conducted on the human in a temperature-controlled room. In experiments on the finger it was found necessary to place the bottom half of a balloon over the flange of the measuring capsule with a hole in the balloon to receive the finger. The area was thus not known in this latter case. Blood flow through the finger was determined by standard plethysmograhic methods (water-filled plethysmograph and tambour recording).

Table I. *The effect of venous congestion and complete occlusion on T.W.L.*

Subject	T.W.L. (mg/area/ 3 min)	E. T. (°C)	S. T. (°C)	R. H. (%)	Area	Remarks
1	1.50	21.8	24.8	44	Right	Normal
	1.27				middle	V.O. 75
	1.23				dorsal	C.O.
	1.05					r.h.
	1.31					V.O. 75
	1.13					After V.O. 75
2	1.40	23.5	52	52	Right	Normal
	1.51				middle	V.O. 75
	0.99				dorsal	After V.O. 75
	1.13					C.O.
	0.79					r.h.
3	1.87	20.7	25.5	39	Right	Normal
	1.76				middle	V.O. 75
	1.12				dorsal	After V.O. 75
	1.23					C.O.
	1.03					r.h.
4	0.98	21.2	30.3	39	Right	Normal
	1.42				middle	V.O. 75
	1.34				dorsal	After V.O. 75
	1.24					C.O.
	1.15					r.h.
5	0.53	18.2	22.5	39	Right	Normal
	0.51				middle	V.O. 75
	0.34				dorsal	After V.O. 75
	0.46					C.O.
	0.23					r.h.
6	0.93	21.2	28.7	31	Right	Normal
	0.81				middle	V.O. 75
	0.70				dorsal	After V.O. 75
	0.67					C.O.
	0.32					r.h.
7	1.37	22.1	23.2	28	Right	Normal
	0.63				fore	V.O. 75
	0.40				ventral	After V.O. 75
	0.65					C.O.
	0.22					r.h.
8	1.41	20.6	26.9	30	Right	Normal
	0.83				middle	V.O. 75
	0.54				ventral	After V.O. 75
	0.65					C.O.
	0.32					r.h.

Venous or arterial occlusion were performed with a standard sphygmomanometer. The plethysmograph and balloon-covered capsule were fitted to separate joints of the same finger.

Environmental temperature (E.T.) and relative humidity of the air (R.H.) were registered with standardized wet and dry bulb mercury thermometers. Skin temperature (S.T.) was recorded with thermistor units or with a Thermatron HM-202P (Zeniter-Heiwa Electronic Industrial Co.) Atropinization of the area under investigation was achieved according to the method of Bettley & Grice (1) and microscopic examination showed that no sweat formed on the area under the existing environmental conditions.

RESULTS

A. *The effect of venous congestion and complete occlusion*

These experiments were conducted on the finger and toe. The water loss measuring capsule was attached to the proximal part of the finger and the plethysmograph to the distal part of the same extremity. In this way the blood flow changes produced by inflation of the sphygmomanometer cuff could actually be visualised whilst measuring T.W.L. Table I shows the results obtained but it must be borne in mind that the area used is not known but is constant for any one experiment. Measurements were made at intervals of 3 minutes. (In the tables, C.O. signifies complete arterial occlusion at 180 mmHg; V.O. 75, venous occlusion at 75 mmHg; after V.O. 75, after release of V.O. 75; r.h., reactive hyperaemia after release of C.O.).

From Table I it can be seen that venous congestion usually brings down the value of transepidermal water loss, though in some cases an increase can be observed. After venous congestion has been released, we find an increase in blood flow (Table VI) and a corresponding decrease in T.W.L. Complete occlusion also brings the value of T.W.L. down, and in many cases this value is slightly higher than that obtained after release of venous congestion. During reactive hyperaemia we find a massive increase in flow (Table VI) and a corresponding large decrease in T.W.L. This latter value was found to be the lowest of all values of T.W.L. in any given experiment.

B. *Changes in T.W.L. produced by a moderate increase in venous pressure (10–35 mmHg)*

In this case the pressure of the manometer was varied in the range 10–35 mmHg. The changes recorded in T.W.L. are shown in Table II.

There is a consistent increase in T.W.L. if the venous pressure is increased up to 30 mmHg. After this a decrease is observed (at 40 mmHg). This is the reverse of what was reported in the previous section, where venous congestion (40–90 mmHg) usually produced a decrease under the same environmental conditions.

C. *The effect of a change in tone on the value of T.W.L.*

In this series of experiments the tone of the vessels in the fingers was altered by placing the opposite hand into either cold or hot water. This was maintained until the reaction in the test hand could be observed on the plethysmograph tracing (5 min). The experimental arrangement was similar to that of the previous section and the dorsal side of the finger was used.

Table III shows that cold water application to the other hand results in either an increase or a decrease in T.W.L. The same results are found if warm water is applied to the contralateral hand and it is thus clear that marked changes in T.W.L. can be obtained by physiologically changing the state of the circulation in the skin.

D. *The influence of bloodless fields on T.W.L.*

Bloodless fields were created on the arm or leg by wrapping a rubber bandage tightly around the extremity starting at either the toes or the fingers (Bier's bandage). T.W.L. measurements were then immediately taken on the bloodless area and Table IV shows the results obtained. T.W.L. again shows either an increase or a decrease with a bloodless field. Another interesting point is the fact that a bloodless field gives a higher T.W.L. value than that obtained with C.O. The former value was found to be nearer to those obtained with venous congestion.

Table II. *The effect of a moderate increase in venous pressure on T.W.L.*

Subject	T.W.L. (mg/5 cm²/ 3 min)	E.T. (°C)	S.T. (°C)	R.H. (%)	Area	Remarks
1	0.48	21.5	30.3	39	Right calf	Normal
	0.66		30.3			10 mmHg
	0.73		30.3			20 mmHg
	0.53		29.7			30 mmHg
2	0.60	21.9	30.3	32	Left calf	Normal
	0.70		30.2			10 mmHg
	0.73		30.2			20 mmHg
	0.95		30.2			30 mmHg
	0.85		29.1			40 mmHg
3	0.42	22.1	30.8	32	Left calf	Normal
	0.55		30.8			10 mmHg
	0.66		30.8			20 mmHg
	0.75		30.6			30 mmHg
	0.50		30.2			40 mmHg
	0.51		29.9			50 mmHg

Table III. *The effect of a change in tone on T.W.L.*

Subject	T.W.L. (mg/area/ 3 min)	E. T. (°C)	S. T. (°C)	R. H. (%)	Area	Remarks
1	2.58	17.8	26.5	52	Right middle	Normal
	2.65		26.5			Cold water 17.5°C
	1.78		26.4			Warm water 42.2°C
2	1.96	23.0	27.5	27	Left middle	Normal
	2.33		28.9			Cold water 3.5°C
	2.27		34.0			Warm water 42.5°C
	2.30		34.2			Warm water 41.0°C
	2.22		33.8			Cold water 16.8°C
3	1.35	21.2	22.5	42	Left middle	Normal
	1.89		22.5			Cold water 3.5°C
	1.94		25.8			Warm water 42.0°C
	2.44		25.0			Cold water 13.0°C

E. *T.W.L. values obtained with the white line and triple response*

The triple response of Lewis and the white line provided an excellent experimental procedure for investigating the effect of vascular changes on water loss. The white line and triple response were obtained with appropriate pressure from a blunt instrument and Table V shows that there is a consistent and significant decrease in T.W.L. over a (histamine)? wheal. An important finding hence is that complete occlusion and reactive hyperaemia can bring this value down still further under these environmental conditions. The white line also brings the value down. The red line, which is apparently vasodilation, shows a variable result, which is usually not significantly different from the white line.

Table IV. *The effect of bloodless fields on T.W.L.*

Subject	T.W.L. (mg/5 cm²/ 3 min)	E. T. (°C)	S. T. (°C)	R. H. (%)	Area	Remarks
1	1.30	16.9	32.1	68	Leg	Normal
	0.80					C.O.
	1.05					Bloodless
2	1.00	16.8	31.8	68	Arm	Normal
	0.85					Bloodless
3	0.95	16.8	31.8	68	Leg	Normal
	0.60					Bloodless
4	0.59	17.5	31.5	56	Arm	Normal
	0.49					Bloodless
5	0.50	19.5	31.3	38	Arm	Normal
	0.65					Bloodless
6	1.20	16.9	32.1	68	Leg	Normal
	0.77					C.O.
	1.01					Bloodless
7	0.50	17.5	31.5	56	Arm	Normal
	0.70					Bloodless

F. The relationship between T.W.L. and blood flow

With these experiments an effort was made to determine the relationship between blood flow and T.W.L. seeing that the previous results indicate that the loss does depend on the presence of blood and/or on blood flow. The human finger was again used exclusively and the experimental arrangement was similar to that reported earlier. Blood flow was determined by venous occlusion plethysmography and although this method has many drawbacks it was used to give an indication of blood flow in cc/min/cc tissue. Blood flow through the fingers was altered by venous congestion, complete occlusion, but mostly by heating (local or generalized body heating). Because relatively high environmental temperatures were used in the latter case, the fingers were again atropinized by iontophoresis. (Preliminary experiments were done to investigate the effect of iontophoresis on blood flow and it was found that no significant changes occur.) A visual check was made with a dissecting microscope to see if the atropinization was effective and it was found that no sweat drops formed on the atropinized finger even at the higher environmental temperatures.

An important point to remember is that T.W.L. was measured on the proximal part of the finger and blood flow was recorded on the distal part (finger tip). Experiments were thus conducted to see whether the blood flow in the proximal and distal parts of the finger differed greatly and it was found that although the blood flow is higher in the tip of the finger, the changes in blood flow produced by various procedures are of similar magnitude. It was thus decided to use this technique to correlate blood flow and T.W.L. The right middle finger was used in all cases.

Table VI shows some of the results obtained and it is clear that T.W.L. does follow blood flow positively, though definitely not in a linear fashion. Any one subject shows that a high value of T.W.L. is associated with a high blood flow value, but if the blood flow is now increased further, T.W.L. may increase or decrease. (All the experiments listed in Table VI were done in the same fashion: the subject was seated in a small airtight room and after a period (half an hour) of acclimatization, the "resting" T.W.L. and blood flow were determined. This presents the first value given for every subject. After this, the heaters were turned on (subjects 4 and 5) and measurements were then made at 5 min intervals. The results in Table VI are also reported accord-

Table V. *T.W.L. values obtained with the white line and triple response*

Subject	T.W.L. (mg/5 cm²/ 3 min)	E. T. (°C)	S. T. (°C)	R. H. (%)	Area	Remarks
1	1.60	24.8	35.5	55	Right calf	Normal
	1.56		35.6			White line
	1.48		35.4			Red line
	1.35		35.3			Wheal
2	1.65	23.8	32.9	71	Right calf	Normal
	1.45		32.8			White line
	1.38		32.8			Red line
	1.30		32.9			Wheal
3	1.31	24.5	34.5	68	Hand Ventral	Normal
	1.18		34.4			White line
	1.19		34.6			Red line
	1.00		34.6			Wheal
4	1.45	23.9	34.4	71	Hand Ventral	Normal
	1.15		34.5			White line
	1.63		34.5			Red line
	1.19		34.2			Wheal
5	1.42	24.0	33.2	68	Right calf	Normal
	1.28		33.0			White line
	1.15		33.1			Wheal
	1.08		33.1			C.O. for 3 min.
	0.93		33.9			r.h.

ingly). There is a lack of correlation between T.W.L. and skin temperature. It is thus obvious that volume flow (blood flow) is not the only factor of importance here. Vasodilation (produced by heating) can either decrease or increase T.W.L. but the initial increase in blood flow to the fingers (after the heaters were turned on), is always associated with a decreased T.W.L. After this, further vasodilation is observed (plethysmographic results), and this is generally associated with increased T.W.L. After a fairly steady state has been reached, fluctuations in blood flow occur and this is not followed by T.W.L.

DISCUSSION

The experiments reported in this paper show conclusively that the circulation does indeed have a profound effect on T.W.L. and might actually provide the fluid for T.W.L. (bloodless field experiments). Reactive hyperaemia, irrespective of origin, whether complete occlusion or venous congestion, always decreases the value of T.W.L. and, after venous congestion, sometimes produces a T.W.L. value that is lower than that produced by reactive hyperaemia resulting from complete occlusion. The tissue mediators which control reactive hyperaemia to a large extent (3) probably do not leave the skin microcirculation unchanged. From his studies Zweifach (18) concluded that the structural pattern of the cutaneous circulation was atypical, since it was composed predominantly of highly reactive venous vessels. The circulation in the skin appears to be regulated locally by tissue mediators (18). These atypical vessels will influence the level of T.W.L. in an unknown way. The explanation of the paradoxical effects observed in this study as to why a thermoregulatory vasodilation produces an increase in T.W.L. (Table VI) and why a passive dilation resulting from increases in venous pressure (Table I) sometimes produces an increase and sometimes a decrease must therefore await further knowledge of the skin circulation before they can be explained. Some of the results reported in Table V concerning the white line and triple response also fall into this category.

The skin vessels are apparently very sensitive to temperature (17). Hattingh (6) has shown that a poor correlation exists between skin temperature and T.W.L. ($r = 0.262$). Vascular changes in the skin influence T.W.L. and apparently the changes observed with the various experimental procedures reported in Table VI result from modifications in the blood flow through the various components of the skin circulation. This could mean that the vessels under a local area of

Table VI. *Blood flow and Transepidermal water loss*

Subject	T.W.L. (mg/area/3 min)	E.T. (°C)	S. T. (°C)	R. H. (%)	Blood flow (cc/min/8 cc tissue)	Remarks
1	2.06	22.3	33.1	59	0.70	Normal
	0.80		34.3		0.46	Normal
	0.78		34.6		0.43	Normal
	1.70		33.5		—	V.O. 75
	1.18		33.7		0.75	After V.O. 75
	0.74		32.4		—	C.O.
	0.60		33.9		0.85	r.h.
	2.46		32.0		0.55	Normal
2	2.14	22.1	31.8	66	0.44	Normal
	1.68		32.2		0.32	Normal
	1.70		31.5		0.56	Normal
	2.94		30.2		—	V.O. 75
	2.06		31.7		0.65	After V.O. 75
	2.68		29.7		—	C.O.
	1.81		30.9		9.79	r.h.
3	4.50	25.8	32.8	42	0.36	Local heating
	5.50		35.2		0.40	Local heating
	4.72		36.1		0.43	Local heating
	5.80		36.4		0.34	Local heating
	4.95		36.5		0.40	Local heating
4	3.60	35.8	34.4	43	0.88	Generalised body heating
	4.40		35.8		1.00	
	6.10		36.1		1.30	
	5.80		36.9		0.48	
	6.40		37.1		—	C.O.
	5.70		37.2		1.52	r.h.
	6.55		37.2		—	V.O. 75
	5.89		37.3		1.20	After V.O. 75
5	4.15	39.5	35.3	34	0.60	Generalised body heating
	4.47		35.5		0.72	
	5.45		36.4		0.8[illegible]	
	6.15		37.0		0.72	
	6.32		37.2		—	C.O.
	5.10		37.3		0.98	r.h.
	6.35		37.2		—	V.O. 75
	5.75		37.3		0.74	After V.O. 75

investigation respond to the altered conditions produced by the measuring technique. There is thus a likelihood of strong central and reflex control systems regulating this local area of the skin circulation. These systems would react on information from the area under the capsule and the result would be a change in T.W.L. The anomalous results observed depend, therefore, on which system (central or reflex) has the overriding power. We therefore require wider knowledge of this particular vascular bed to explain some of the effects observed.

A further point of interest from Table VI is that venous congestion and complete occlusion always produce an increase above the resting level of T.W.L. in the generalized heated subjects. If we presume that the fluid for T.W.L. comes from the blood we can argue that so much fluid is released that the normal mechanisms drawing fluid back into the vascular system are insufficient and we thus find this increase under complete or venous occlusion. Normally, we could thus have a mechanism forcing the fluid out of the vascular system and one pulling the surplus back. The system forcing out fluid would presumably be the blood pressure and the one drawing back would then be the colloid osmotic pressure of the plasma proteins. The balance between these two factors would, therefore, be critical and under colder environmental conditions one could argue that only a little less fluid is "reabsorbed" than is "secreted" and the surplus is then available for T.W.L. During warmer environmental conditions more fluid is made available, due to thermoregulatory bloodflow changes in the skin microcirculation and here the tonus of the vessels as well as the minute flow seem to be important.

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