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RELATIONSHIP BETWEEN A RANGE OF TISSUE TEMPERATURE AND LOCAL OXYGEN UPTAKE IN THE HUMAN FOREARM. I. CHANGES OBSERVED UNDER RESTING CONDITIONS [1, 2]

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The advent of the use of hypothermia as an adjunct to surgery has revived interest in the effect of alterations of local temperature on tissue metabolism. In the early part of this century, several investigators (1, 2) performed *in vitro* studies and found that increasing the temperature of muscle slices raised their oxygen consumption, while an opposite effect was produced by decreasing the temperature. The Q_{10} of this relationship was generally found to be slightly above the value of two (2). However, one limitation of the work was that the absolute oxygen consumption was closely dependent upon the composition of the bath in which the tissue was suspended.

In more recent years a number of workers (3–5) have noted an increase in local circulation with exposure of a limb to high external temperatures and a decrease with cooling of the tissues. From such evidence it has been concluded that the alterations in blood flow produced by local heat and cold are due both to the direct action of these agents on the blood vessels and to changes in the metabolic needs of the tissues being supplied. However, it is apparent that data on the circulation alone are not sufficient for the determination of tissue oxygen utilization, and that for this purpose, the simultaneous measurement of the quantity of oxygen removed from the blood as it passes through the structures under study is likewise essential.

Studies on the effect of hypothermia on the whole organism have also contributed to the elucidation of the problem. In the rat (6) and in the dog (7, 8) this state is associated initially with a rise in oxygen consumption, corresponding to a stress reaction developed in the body, and then a fall as cooling is continued. If shivering, which is elicited in the first phase, is prevented by the use of barbiturates, the increase in oxygen consumption is no longer observed (7). In poikilothermic animals hypothermia produces only a reduction in oxygen consumption (9).

The purpose of this paper is to present the effects of local heating and cooling on the resting oxygen uptake of the tissues of the forearm.

METHOD

The investigation was performed on 17 healthy subjects between the ages of 19 and 51 years. Thirteen were males and four were females. In all, 27 experiments were done, their duration averaging six hours. In this period no food was served to the subject other than one or two small chocolate bars.

Three different procedures were carried out during each experiment: *1*) blood flow recordings on a six inch segment of forearm enclosed in a venous occlusion plethysmograph, according to the technique previously described [3] (10) (Figure 1); *2*) determinations of oxygen content of venous blood from deep or superficial veins of the forearm; and *3*) studies of muscle, subcutaneous tissue, skin, and rectal temperatures, using thermocouples. The temperature of the water in the plethysmograph (bath temperature) was first maintained at 45° C. and then lowered to 32° and finally to 17°,[4] and at each level all of the above procedures were done, together with blood pressure and pulse rate readings, obtained from the opposite extremity.

[1] This investigation was supported in part by Research Grant H-2568 from the National Institutes of Health, United States Public Health Service.

[2] This paper was presented at the International Cardiovascular Society meeting at San Francisco, Calif., on June 21, 1958.

[3] A modification of the method consisted of the use of an air reservoir with appropriate valves for the application of a venous collecting pressure. With such an arrangement a delay of somewhat more than a second occured in the build-up of the pressure in the cuff to the desired level, thereby practically eliminating artifacts in the blood flow record (Figure 1).

[4] Five pilot studies revealed that altering the sequence in which the forearm was exposed to the different bath temperatures did not materially affect the results.

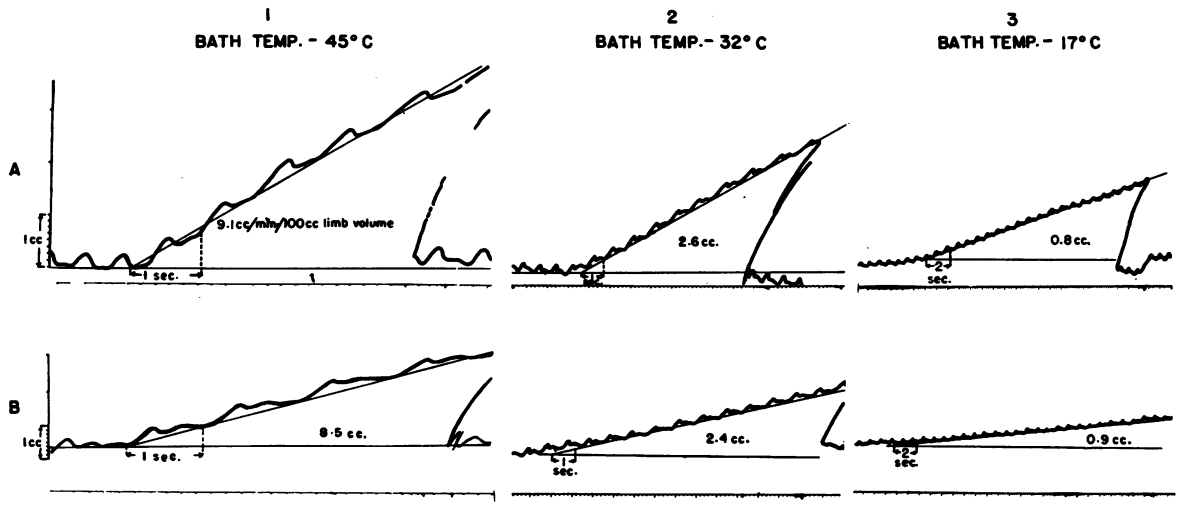

FIG. 1. RESTING BLOOD FLOW CURVES OBTAINED FROM THE FOREARM AT THREE DIFFERENT BATH TEMPERATURES, USING A VENOUS COLLECTING PRESSURE OF 60 MM. HG APPLIED TO THE ARM

Arterial occlusion pressure was maintained at the wrist before and during period of blood flow recording to prevent vascular changes in the hand from influencing readings obtained from the forearm. Calibration scale, in cubic centimeter divisions, to the left of the curves, was derived by introducing increments of 1 cc. of water into the plethysmograph with the forearm in position but with the circulation occluded. Blood flow, in cc. per minute per 100 cc. limb volume, was calculated on the basis of the height of the volume curve reached in first second of application of venous collecting pressure. Two seconds was frequently used in the case of bath temperature of 17° C. because of relative slowness of ascent of blood flow curve. A = Subject S. M.; B = Subject A. L.

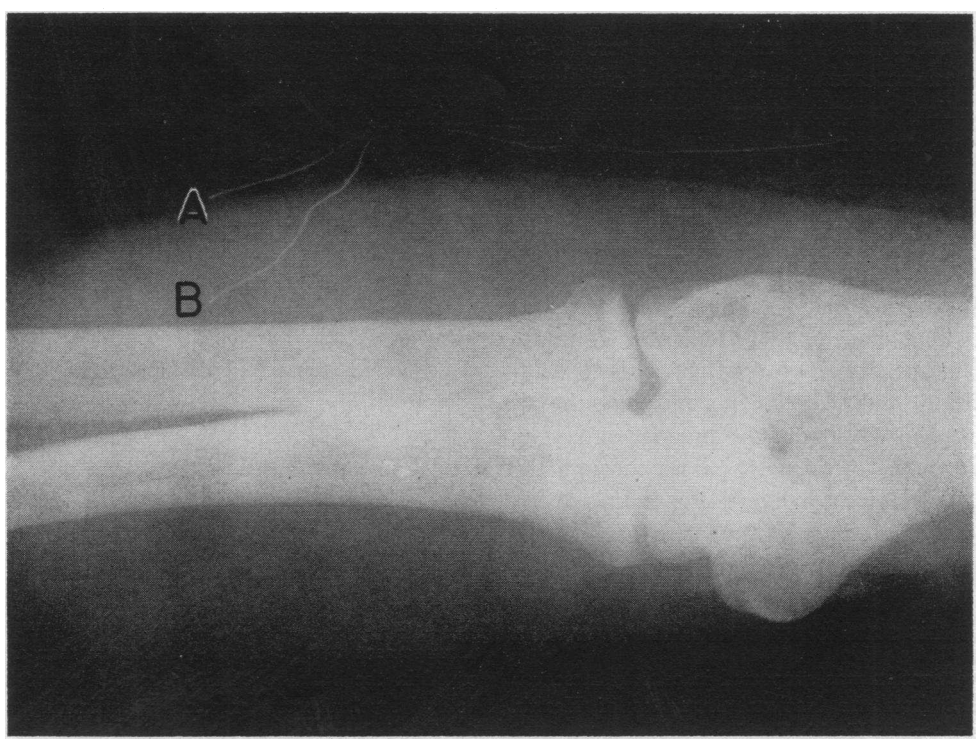

FIG. 2. SOFT TISSUE X-RAY SHOWING THERMOCOUPLES IN PLACE

A = subcutaneous tissue thermocouple. B = muscle thermocouple, with tip near the bone. Skin thermocouple, lying on the skin, is not clearly visualized.

The experiments were performed in a temperature-regulated room, with the temperature ranging between 22 and 25° C. and the humidity around 50 per cent. Psychic stimuli which could conceivably alter local circulation were kept at a minimum. The subject, dressed in a surgical gown, lay in the supine position during the entire experimental period. Care was taken to support the forearm at heart level in a constant position and angle with regard to the long axis of the body (11, 12).

Thermocouples were constructed of fine constantan and insulated copper wires completely enclosed in polyvinyl tubing (No. 442-T, Becton, Dickinson). The reference junction was immersed in a thermos jar filled with ice. The output of the thermocouples was recorded by means of a sensitive potentiometer calibrated to read directly in degrees centigrade.

Using aseptic technique and local anesthesia with 2 per cent procaine, a thin-walled No. 18 needle (3.7 cm. long) with obturator was inserted for a depth of approximately 3 cm. into the brachio-radialis muscle of the forearm. The obturator was then removed, a thermocouple was passed through the full length of the needle, and the latter was carefully withdrawn, leaving the thermocouple in place.[5] In a similar manner, a thermocouple was inserted into the subcutaneous tissue, parallel to the skin, for a distance of about 3 cm., while a third one was attached to the skin by rubber cement in the vicinity of the other two (Figures 2 and 3). A fourth modified thermocouple was inserted into the rectum for approximately 6 to 7 cm.

Blood samples for the determination of venous oxygen content were obtained from a vein in the antecubital space and analyzed according to the manometric method of Van Slyke. The technique used was as follows: First, under sterile precautions, a No. 18 thin-walled needle, pointed distally, was inserted into the vein. Then the free end of a sterile-silicone treated polyethylene catheter (PE 50, Clay-Adams), attached to a special metal coupler (PE 2625A, Clay-Adams), was threaded through the needle into the vessel for a distance of 5 to 8 cm., so that the tip lay in the mass of forearm subsequently enclosed by the plethysmograph. Following this the needle was withdrawn from the vein, leaving the tubing in place.[6] Blood samples were obtained according to the plan outlined in Figure 3.

No attempt was made to collect repeated arterial blood samples, but instead comparable data were derived by re-oxygenating venous blood and determining in duplicate total oxygen capacity. From this figure arterial oxygen content was calculated (13), on the basis that arterial blood is 98 per cent saturated with oxygen (14). Since

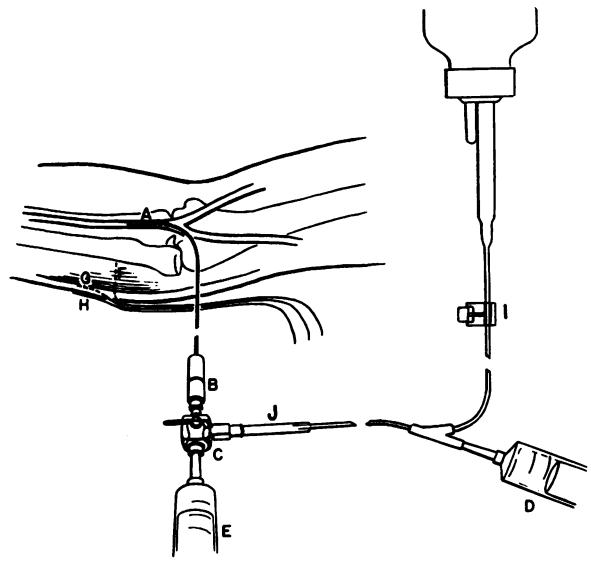

FIG. 3. STEPS IN THE COLLECTION OF A BLOOD SAMPLE

1) Apply and maintain arterial occlusion pressure at wrist for three to four minutes to prevent vascular changes in hand from influencing venous content of blood from forearm; *2*) close clamp I; *3*) aspirate fluid in tubing, using syringe D, until blood appears in side arm J; *4*) rotate handle of stopcock C 90 degrees so as to allow a drop of blood to drain away from free female opening; *5*) attach oiled syringe E, with dead space filled with a solution of heparin and sodium fluoride, to free opening and withdraw 3 cc. of blood in approximately 10 seconds; *6*) disconnect syringe, cover tip with metal cap and rotate rapidly to mix blood with anticoagulant; *7*) flush entire infusion system with saline containing heparin and then allow small quantity to enter vein continuously between blood sample collections. A = cannula in vein directed toward hand; B = special adapter for cannula. F, G, and H = muscle, subcutaneous tissue and skin thermocouples, respectively.

all the subjects used in the study were normal, with no signs of cardiac or pulmonary pathology, such an assumption was considered valid. Furthermore, the data for the three bath temperatures were collected during the course of the same experiment, with the subject under constant environmental conditions and in approximately an unaltered physiologic state. The possibility, therefore, that a change in the oxygen content of arterial blood could have occurred in the course of the experimental period appeared unlikely.

The plan utilized in each experiment was as follows: First, a polyethylene tube was passed into a deep or superficial vein and connected to an infusion set (Figure 3). Then the various thermocouples were inserted into their respective sites and the wires directed toward the arm (Figure 3). Finally the forearm was passed into the plethysmograph, with the thermocouple wires being let out of the proximal opening parallel to the skin, and the openings were made water-tight according to the technique

[5] In each instance the length of thermocouple in the tissues was determined at the end of the experiment. This was found to be an average of 3.5 cm., with a range of 1.8 cm. to 5.1 cm.

[6] In a number of instances, at the end of the experiment the cannulated vein was filled with radiopaque material through the polyethylene tube, and a soft-tissue X-ray was taken (Figure 4).

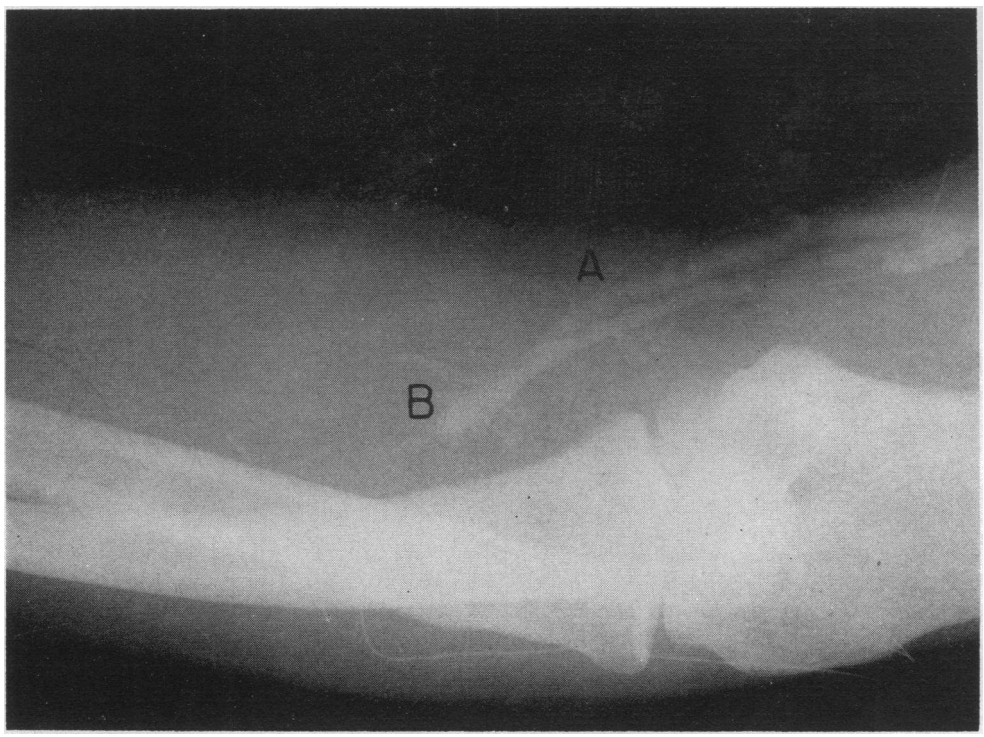

FIG. 4. CANNULATED VEIN OUTLINED WITH RADIOPAQUE SUBSTANCE

A = polyethylene cannula in vein; B = obstruction to distal movement of the material, probably because of the presence of a valve. Proximal portion of vein was filled with radiopaque substance. Thermocouples are seen in lower portion of the figure.

previously described (10). The next step was to fill the plethysmograph with water at a temperature of 45° C., which level was maintained for approximately 90 minutes until the various measurements became constant. Following this a series of five or six temperature and blood flow determinations was obtained, and, after a delay of two minutes, a blood sample was collected (15). The sequence of temperature and blood flow readings and blood sampling was repeated at least three or four times over the course of the next hour. In the first six experiments duplicate tests were run on each of the three to five blood samples, while in the remainder this was done only when the reading was not in accord with the other data obtained under the same conditions.

As soon as the above determinations were made, the plethysmograph was emptied of hot water and filled with water at a temperature of 32° C. The exact sequence described above was again carried out at this bath temperature, and then at a bath temperature of 17°, the latter condition being maintained through the use of a refrigeration system connected to a series of coils in the interior of the plethysmograph. With each of the two bath temperatures, the various measurements were obtained only after a period of 90 minutes had elapsed, in order to permit stabilization of the circulation at the new level.

Of the 27 experiments performed, in 17, blood samples were collected from a deep vein and in 10, from a superficial vein. However, it should be pointed out that at times it was difficult to identify with certainty the type of vessel cannulated. Furthermore, there was no way of determining whether an apparently superficial vein did not receive communicating vessels from the deep venous system and a deep vein, tributaries from the superficial venous system distal to its subcutaneous location.

RESULTS

From the collected data, resting oxygen uptake was calculated using the Fick principle (16). For the derivation of an average tissue temperature, the temperature readings at each of the three bath temperatures were weighted on the basis of the contribution of the tissue from which they were obtained to the total vascular mass of the forearm [combined skin and subcutaneous tissue, 17.4 per cent by weight; muscle, 82.6 per cent (17)].

Systemic changes

Pulse rates showed no consistent change at the different bath temperatures. In most instances the

readings were the same for the three experimental conditions, in some they were lowest at a bath temperature of 17° C., while in others they were lowest at a bath temperature of 45°. Blood pressure readings also showed no consistent or definite trend. At a bath temperature of 45° about one-half the subjects experienced a generalized sensation of warmth and sweating, due to reflex vasodilatation, while at bath temperatures of 32° and 17° no symptoms were noted. The average rectal temperature at the three bath temperatures varied between 37.3 and 37.7°.

Changes in blood oxygen

The mean derived oxygen content of arterial blood for all the subjects was 20.20 volumes per cent. The oxygen content of blood from deep veins showed a progressive decrease as the bath temperature was lowered (an average of 15.52, 12.78 and 10.62 volumes per cent at 45°, 32° and 17°, respectively), these alterations being reflected in a reverse trend in the case of the oxygen arteriovenous difference (an average of 4.79, 7.62 and 9.77 volumes per cent at 45°, 32° and 17°, respectively). A similar type of relationship was noted for the oxygen content of blood from superficial veins (an average of 16.18, 11.12 and 10.46 volumes per cent at 45°, 32° and 17°, respectively), and for the oxygen arteriovenous difference (an average of 3.73, 8.88 and 9.45 volumes per cent at 45°, 32° and 17°, respectively).

Changes in blood flow

For the group as a whole the average blood flow at a bath temperature of 45° C. was 7.3 cc. per minute per 100 cc. of limb volume; at a bath temperature of 32° it was 2.3 cc.; while at a bath temperature of 17° it was 0.7 cc.

Changes in oxygen uptake

Examination of Table I reveals that on the basis of blood obtained from deep veins, the calculated oxygen uptake at an average tissue temperature of 39.0° C. was 0.369 cc. per minute per 100 cc. limb volume, as compared with 0.199 cc. at an average tissue temperature of 35.4°, and 0.071 cc. at an average tissue temperature of 26.9°. When the data were subjected to statistical analysis, it was found that the probability that the difference between the results at average tissue temperatures of 39.0° and 35.4° arose simply by chance variation was less than 0.1 per cent ($p < 0.001$) (18). The probability that the difference between the figures obtained at average tissue temperatures of 35.4° and 26.9° was on the basis of sampling variation alone was also less than 0.1 per cent ($p < 0.001$).

Examination of Table II reveals that on the basis of blood obtained from superficial veins the oxygen uptake at an average tissue temperature of 38.9° C. was 0.261 cc. per minute per 100 cc. limb volume, as compared with 0.165 cc. at an average tissue temperature of 34.9°, and 0.070 cc. at an average tissue temperature of 26.7°. Statistical analysis of the data demonstrated that the probability that the difference between the results at average tissue temperatures of 38.9° and 34.9° arose simply by change variation was less than 1 per cent ($p < 0.01$). The probability that the difference between the figure obtained at average tissue temperatures of 34.9° and 26.7° was on the basis of sampling variation alone was also less than 1 per cent ($p < 0.01$).

DISCUSSION

There seems to be little question that in the present study raising the average temperature of the structures of the forearm by the surface application of heat produced an increase in oxygen uptake, while cold had an opposite effect (Tables I and II). This relationship held regardless of whether the venous blood used in the determination of the oxygen arteriovenous difference came from deep or superficial veins. Furthermore, the changes appeared to be due primarily to local alterations in the tissues, the systemic responses elicited by the different experimental conditions being minimal and inconstant.

It is necessary to point out, however, that at the high bath temperature the average oxygen uptake calculated on the basis of blood obtained from superficial tissues was less than that derived from oxygen content of blood draining deep tissues (0.261 cc. per minute per 100 cc. limb volume, as compared with 0.369 cc.). A possible explanation for such a difference is the following: Due to the proximity of the skin to the source of the heat, the cutaneous circulation was markedly en-

hanced, resulting in a large oxygen content of venous blood draining superficial tissues and a small oxygen arteriovenous difference (3.73 volumes per cent). At the same time, however, this augmented circulation was not reflected proportionately in the total blood flow figure, since the latter was the

TABLE I

Effect of different bath temperatures on resting oxygen uptake of the forearm based on blood samples from deep veins

Subject	O_2 capacity *cc./100 cc. blood*	Cal. art. O_2 *cc./100 cc. blood*	Venous O_2 *cc./100 cc. blood*	O_2 A. V. diff. *per cc. blood*	Blood flow *cc./min./ 100 cc. vol.*	O_2 uptake *cc./min./ 100 cc. vol.*	Temp. ° C. Skin	Subcutaneous tissue	Muscle	Average tissue	Rectal
Bath temperature—45° C.											
O. C.	21.76	21.32	17.57	0.0375	8.8	0.330	40.2	40.1	39.4	39.5	38.2
S. M.*	21.26	20.84	15.02	0.0487	9.4	0.544	41.0	39.0	37.8	38.2	37.5
H. H.	20.00	19.60	16.46	0.0314	8.9	0.279	41.5	40.1	37.6	38.2	37.1
S. T.*	19.77	19.37	15.84	0.0353	6.3	0.222	42.5	41.5	38.6	39.2	37.4
J. T.*	21.89	21.45	17.94	0.0351	6.7	0.235	40.8	40.6	38.3	38.7	37.5
A. K.†	21.57	21.14	17.90	0.0324	6.6	0.214	41.6	39.9	38.9	39.2	37.9
G. T.	19.64	19.25	15.29	0.0396	3.7	0.146	43.0	41.3	40.7	40.9	39.1
A. P.	21.37	20.94	11.11	0.0983	5.6	0.550	42.7	39.6	38.5	38.9	36.9
A. M.	18.00	17.64	11.91	0.0573	12.7	0.728	41.5	39.8	38.2	38.6	37.5
A. L.	20.49	20.08	13.90	0.0618	8.1	0.501	41.8	39.6	38.7	39.0	38.3
G. B.	23.06	22.60	16.82	0.0578	6.3	0.364	42.5	42.3	37.8	38.6	37.7
H. B.	20.98	20.56	16.54	0.0402	7.8	0.314	41.1	40.9	38.4	38.8	38.1
Mean	20.81	20.39	15.52	0.0479	7.6	0.369	41.7	40.4	38.6	39.0	37.7
Standard error				±0.0055	±0.6	±0.051					
Bath temperature—32° C.											
O. C.	21.76	21.32	12.82	0.0850	2.9	0.246	34.4	35.4	35.5	35.4	38.2
S. M.*	21.26	20.84	13.40	0.0744	2.8	0.208	33.2	34.1	35.7	35.2	37.0
H. H.	20.00	19.60	14.61	0.0499	4.0	0.200	33.3	34.0	35.9	35.5	36.7
S. T.*	19.77	19.37	14.02	0.0535	1.7	0.091	33.1	33.0	35.3	34.9	37.5
J. T.*	21.89	21.45	14.91	0.0654	1.9	0.124	32.5	33.2	35.6	35.1	37.3
A. K.†	21.57	21.14	13.22	0.0792	1.7	0.135	33.3	33.7	35.4	35.1	37.7
G. T.	19.64	19.25	12.29	0.0696	1.6	0.111	33.6	33.0	35.9	35.4	37.3
A. P.	21.37	20.94	9.74	0.1120	2.7	0.302	33.1	34.4	34.6	34.4	36.8
A. M.	18.00	17.64	10.18	0.0746	4.8	0.358	33.7	34.6	36.0	35.7	37.1
A. L.	20.49	20.08	10.12	0.0996	2.5	0.249	33.4	34.4	36.7	36.2	38.2
G. B.	23.06	22.60	15.66	0.0694	2.5	0.173	33.0	33.8	36.5	36.0	37.3
H. B.	20.98	20.56	12.40	0.0816	2.4	0.196	34.9	34.7	37.2	36.8	37.9
Mean	20.81	20.39	12.78	0.0762	2.6	0.199	33.4	34.0	35.8	35.4	37.4
Standard error				±0.0051	±0.3	±0.023					
Bath temperature—17° C.											
O. C.	21.76	21.32	12.75	0.0857	1.0	0.086	23.9	21.6	26.3	25.7	38.1
S. M.*	21.26	20.84	11.62	0.0922	0.8	0.074	18.7	21.1	27.5	26.2	36.9
H. H.	20.00	19.60	12.59	0.0701	0.7	0.049	18.3	19.7	29.8	27.9	36.6
S. T.*	19.77	19.37	12.55	0.0682	0.6	0.041	24.3	24.1	28.3	27.6	37.3
J. T.*	21.89	21.45	11.48	0.0997	0.5	0.050	18.3	18.3	27.1	25.6	37.1
A. K.†	21.57	21.14	11.30	0.0984	0.7	0.069	19.1	21.0	26.0	24.9	37.6
G. T.	19.64	19.25	9.37	0.0988	0.6	0.059	21.8	22.8	29.8	28.5	37.3
A. P.	21.37	20.94	9.45	0.1149	1.0	0.115	18.3	20.0	25.5	24.4	36.6
A. M.	18.00	17.64	6.96	0.1068	0.8	0.085	19.6	21.2	27.5	26.3	36.8
A. L.	20.49	20.08	7.99	0.1209	0.7	0.085	19.5	21.4	27.3	26.1	38.1
G. B.	23.06	22.60	10.69	0.1191	0.6	0.071	18.5	19.6	32.9	30.5	37.3
H. B.	20.98	20.56	10.76	0.0980	0.7	0.069	20.4	20.0	31.8	29.8	37.7
Mean	20.81	20.39	10.62	0.0977	0.7	0.071	20.1	20.9	28.3	26.9	37.3
Standard error				±0.0049	±0.1	±0.006					

* Average of two experiments.
† Average of three experiments.

TABLE II

Effect of different bath temperatures on resting oxygen uptake of the forearm based on blood samples from superficial veins

Subject	Bath temperature—45° C.		Bath temperature—32° C.		Bath temperature—17° C.	
	Average tissue temp.	O_2 uptake *cc./min./ 100 cc.vol.*	Average tissue temp.	O_2 uptake *cc./min./ 100 cc. vol.*	Average tissue temp.	O_2 uptake *cc./min./ 100 cc. vol.*
O. C.	39.5	0.328	35.4	0.281	25.7	0.095
S. M.*	38.0	0.383	35.0	0.159	25.8	0.060
S. L.	39.4	0.115	33.7	0.101	24.3	0.050
A. P.	38.9	0.279	34.4	0.225	24.4	0.105
J. J.	38.9	0.117	36.1	0.055	29.9	0.040
D. A.*	39.0	0.345	34.5	0.189	27.0	0.107
B. K.	38.6	0.391	35.3	0.200	27.1	0.039
M. B.	39.1	0.131	35.1	0.109	29.1	0.061
Mean	38.9	0.261	34.9	0.165	26.7	0.070

* Average of two experiments.

resultant of vascular changes not only in the superficial tissues, but also in muscles, in which the vasodilating effect of the surface heat was not as great. It would be expected, therefore, that an oxygen uptake figure derived from an oxygen arteriovenous difference which was too low to represent changes in the total vascular tissue would be smaller than the true value.

In regard to the calculation of oxygen uptake based on blood draining deep tissues, the situation was reversed. Under these circumstances a higher oxygen arteriovenous difference was obtained (4.79 volumes per cent), due to the relatively slower circulation in the muscles, while at the same time the figure for total blood flow more than reflected the vascular changes in this tissue because of the contribution of the markedly enhanced cutaneous circulation. Hence, an oxygen uptake figure derived from such data would most likely be greater than the true value.

It would seem, then, that in the case of a high bath temperature, the reported average reading for oxygen uptake based on blood from superficial tissues was probably too low, while that based on blood from deep tissues was probably too high, the true value falling somewhere between the two.

It is of interest to consider possible mechanisms responsible for the differences in oxygen uptake observed under the various experimental conditions. At the highest tissue temperature the increase in oxygen uptake appeared to be satisfied primarily by an augmentation in blood flow, with the oxygen arteriovenous difference actually being smaller than at the two lower tissue temperatures. The latter finding would appear to indicate that the resulting increase in local circulation was greater than adequate to satisfy the higher metabolic needs, and, as a consequence, less than the normal quantity of oxygen was removed from each cc. of blood as it passed rapidly through the tissues. It is understandable why the described changes occurred, since it is generally accepted that heat is a very potent vasodilating agent.

At the low experimental tissue temperature, a reverse situation existed. There was a marked reduction in blood flow, together with a greater removal of oxygen from each cc. of blood. The latter change occurred despite the fact that the rate of oxygen dissociation is reduced at a lower tissue temperature.[7] The finding of an increase in oxygen arteriovenous difference would appear to indicate that the reduction in blood flow was of greater magnitude than warranted on the basis of diminished oxygen uptake, and, as a result, more than the normal quantity of oxygen had to be removed from each cc. of blood as it passed slowly through the tissues. The fact that cold is a very potent vasoconstricting stimulus explains the type of reaction noted at the low tissue temperature.

It would appear, therefore, that the changes in oxygen uptake produced in the tissues of the forearm by the topical application of heat and cold were dependent primarily upon alterations in local blood flow, with the mechanism of removal of oxy-

[7] However, it is necessary to point out that an increased local acidity may be produced at low tissue temperatures because of an inadequate blood flow, and that such a trend would facilitate oxygen dissociation.

gen from the blood playing a secondary and dependent role.

SUMMARY AND CONCLUSIONS

1) The effect of altering the local external temperature on the resting oxygen uptake of the tissues of the forearm was investigated in a series of 27 experiments performed on 17 normal subjects.

2) Oxygen uptake was calculated on the basis of blood flow determinations, using the venous occlusion plethysmographic method, and of studies of local oxygen arteriovenous difference.

3) On the basis of blood obtained from deep tissues, the calculation of oxygen uptake at an average tissue temperature of 39.0° C. (produced by a bath temperature of 45° C.) was 0.369 cc. per minute per 100 cc. limb volume; at a tissue temperature of 35.4° C. (produced by a bath temperature of 32° C.) it fell to 0.199 cc.; while at a tissue temperature of 26.9° C. (produced by a bath temperature of 17° C.), it was only 0.071 cc. The differences at the three levels of tissue temperature were found to be statistically significant.

4) On the basis of blood draining superficial tissues, the calculation of oxygen uptake at an average tissue temperature of 38.9° C. was 0.261 cc. per minute per 100 cc. limb volume, as compared with 0.165 cc. at an average tissue temperature of 34.9°, and 0.070 cc. at an average tissue temperature of 26.7°. These differences were also found to be statistically significant.

It was concluded that raising the local temperature of tissues *in vivo* definitely increased their resting oxygen uptake, while lowering tissue temperature produced a marked reduction in this figure. These results were considered to be in line with the *in vitro* studies on tissue strips and the hypothermia experiments on the whole organism.

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