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ON THE ACCURACY OF THE THERMOSTROMUHR METHOD FOR MEASURING BLOOD FLOW

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The thermostromuhr method for measuring blood flow has been fully described by Rein [1928, 1929*a*, *b*]. Its principles are as follows. High-frequency current is applied by small electrodes at opposite ends of a diameter of the unopened vessel in order to heat the streaming blood within. The temperature rise produced by the current is measured a short way downstream by a thermojunction pressing against the wall of the vessel. The rise in temperature is an inverse function of the blood flow. The measurement of the rise in temperature presents a difficulty because the temperature of the animal's blood may change. To get over this difficulty a second junction is placed upstream to the heated region and connected differentially (or in opposition) with the first (downstream one).

Some difficulties in our early experiments made us suspect that in spite of the use of differential junctions changes in the animal's blood temperature would affect the accuracy of the results. Small blood temperature changes seemed to affect the temperatures of the junctions unequally. The significance of the errors in the flow measurements seemed to depend on the size and rapidity of the blood temperature change and on the junction temperature difference set up by the heating current.

The object of this paper is to describe findings which show that, in some measurements, blood temperature changes may make the method unreliable.

We have not found very much in the literature about rapid changes in blood temperature. In the last century physiologists were interested in the amount of heat given out by different organs and in the conduction of this heat from place to place by the blood stream. Claude Bernard [1876] gives a detailed account of the "topography" of blood temperature in the great vessels. He shows that in animals the temperature of the arterial blood is almost uniform in the great arteries of the trunk and limbs. On the other hand, the temperature of the venous blood in the jugular and femoral veins is about 1° C. below arterial blood temperature. The difference in the arterial and venous blood temperature depends on the temperature of the animal's surroundings. In man several observers, using thermoelectric methods, have found that venous temperature is low and depends on room temperature. Foged [1930] found that the temperature of the blood in the antecubital veins was, on the average, 2·6° C. lower than the rectal temperature. Harris & Marvin [1927] found that the temperature of the blood in the veins on the dorsum of the hand was between 34·3 and 35·8° C. Placing the hand in a water bath, the water being at 25·26° C., lowered the temperature of the venous blood 6·8° C. in 2 min. Wright & Johnson [1932] found that the temperature of the blood in the median cubital, jugular, and saphenous veins was, on the average, 1·2° F. below mouth temperature, the greatest observed difference was 13° F. Such observations, we think, show that changes in the skin circulation, brought about by nervous or chemical means, might cause quite large and rapid changes in venous blood temperature. A rather significant fact shown by Claude Bernard [1852] was that cutting the cervical sympathetic in dogs, cats and horses raised the temperature of the nose and ear passages 3–4° C. in a few minutes.

A rapid rise in blood temperature might be expected in muscular activity. We have not found any blood temperature measurements, but the inference may be drawn from the fact that muscle temperature rises rapidly during activity. Chauveau [1891] found that the temperature of the horses masseter rose 0·42° C. in 10 min. eating, and assumed that the temperature of the blood leaving it rose by the same amount. Béclard [1861] bound a thermometer to the upper arm with many turns of flannel. After about 2 hr. complete rest the temperature became constant to a fiftieth of a degree. A 5 kg. weight was then held for 5 min., the temperature rose 1·35° C. in 10 min. Béclard attributed the rise in temperature to heat production caused by contraction of the biceps. Becquerel & Breschet [1835] put a thermojunction into the fleshy part of the biceps. When the subject was sawing a piece of wood the temperature of the muscle rose 1·0° C. in 5 min. One of us put a thermojunction into the human gastrocnemius; the junction was 7 cm. from the surface. The temperature of the muscle rose 1·5° C. in 1½ min. standing running.

The temperature in the brain and liver has been measured by Crile & Rowland [1922*a*, *b*]. When a rabbit was under nitrous oxide ether was given, the animal struggled and the temperature of its brain fell 2·2° C. in 2 min. Stimulation of the uncut sciatic nerve lowered the temperature of the liver 1·6° C. in half a minute. An unanæsthetized rabbit was given 500 μg. of adrenaline intravenously, a very large dose, and the temperature of its brain rose 1·1° C. in 2 min.

A general survey of this literature shows that some physiological and pharmacological procedures may cause blood temperature changes, especially venous blood temperature changes, amounting perhaps to a degree or more in less than 5 min.

Our results fall into three groups. First, thermostromuhr perfusion experiments. The temperature of the perfusion fluid was altered from time to time and the behaviour of the differential thermojunctions was recorded. These experiments show that changes in the temperature of the perfusion fluid of about 1° C. affected the temperatures of the junctions unequally. Secondly, thermostromuhr experiments on the animal, but without heating the vessel. These experiments show that the changes in the blood temperature caused by adrenaline were large enough to cause unequal heating of the junctions. Thirdly, some experimental work and a discussion on the significance of the errors likely to be found in the flow measurements.

PERFUSION EXPERIMENTS

Method

Each thermoelement has to be calibrated in a perfusion experiment to find the relation between the blood flow and the deflexion of the galvanometer. The technique has been described by Rein [1928, 1929*a*, *b*] and we followed it as closely as possible. A few important details should be mentioned.

Unless otherwise stated, the type of element used was that in which the junctions were joined by a straight piece of constantan wire running along the bottom of the inner wall of the element. This type is referred to by Rein [1928] as "Form III". The important specifications were as follows. The distance between the junctions was at least 2½ times the internal diameter of the element. The distance from each junction to the edge of the element was at least 1 mm. The area of the heating plates in sq. mm. was equal to the internal diameter of the element in mm. The size of the wires forming the junctions was between 0·1 and 0·3 mm. according to the internal diameter of the element. (Rein [1928] used to use junctions of 0·03 mm. wire, he now uses sizes up to about 0·3 mm. [Smyth, 1937].) Each junction was covered with a thin layer of cellulose varnish. The thickness of the element wall varied with the size of the element; for an element of 5 mm. internal diameter it was 1–2½ mm.

The thermocouple galvanometer was made by Downing. Its sensitivity varied according to the amount of magnetic shunting required for critical damping. The sensitivity was about $1 \cdot 2 \times 10^{-7}$ V., $5 \cdot 8 \times 10^{-9}$ A. per mm. at 1 m. Its internal resistance was 19 ohm. Its period was 1·2 sec. The short circuit zero was often checked and varied by less than 1 mm. at 1 m. The usual working distance was 4·5–5 m.

Mr Cowan showed us how to standardize the thermocouple circuit so that the deflexions could be converted into °C. junction temperature difference. This is not usually done, but it has great advantages which will be seen later. According to Hodgman [1933], from data in the *International Critical Tables*, 0·1° C. difference in the temperatures of two copper-constantan junctions sets up an effective e.m.f. of about 4×10^{-6} V. After each experiment 4×10^{-6} V. was put into the thermocouple circuit from a battery and potential divider; this deflexion thus corresponded to about 0·1° C. junction temperature difference. Strictly speaking each couple should have been calibrated separately to get the exact relation between junction temperature difference and e.m.f. This was not done. For our purpose it was sufficient to assume the "ideal" relations between junction temperature difference and e.m.f.

The vessel was perfused by gravity from a 10 l. bottle. The flow was regulated by a screw clip on the tubing leading from the perfusion bottle. It was measured by a stop-watch and measuring cylinder. Except when stated, defibrinated ox blood was used; its temperature was carefully brought to within 0·5° C. of room temperature before the experiment was begun (see later).

Carefully selected pieces of calf, goat, sheep or dog vein were chosen, those with valves or branches were avoided. Special flanged cannulæ were used to avoid irregularities on the inner surface of the perfusion system. Great care was taken to fit a suitable sized element, of slightly smaller diameter than the vessel, nicely round the vein and to fix the leads so that it could not slip. The top of the element and vein were painted with collodion. The thermos flask and vessel were horizontal; the air in the thermos was kept moist by a small piece of wet cotton wool. The height of the outflow tube was adjusted so as to keep the vein under a positive pressure of a few centimetres of water.

A second thermocouple system was used to show changes in the temperature of the perfusion fluid. In some cases one junction was in the air of the thermos flask and the other in the blood a short distance upstream from the element. In others the junctions lay, one on the outer and the other on the inner side of the element wall. The junctions were standardized by the introduction of 4×10^{-6} V. as described above.

In the experiments to be described the heating current was not used and the batteries of the high-frequency generator were disconnected to avoid any escape of stray currents into the thermocouple circuit.

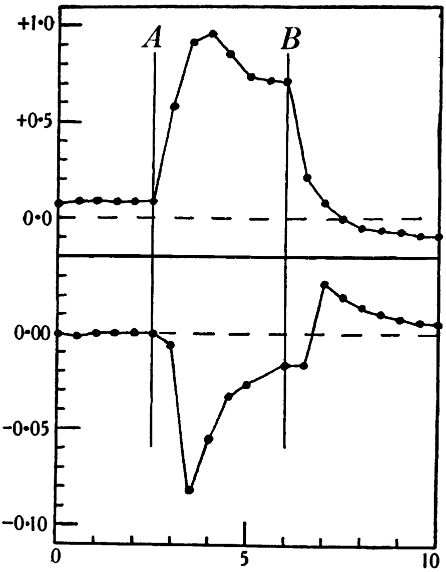

Fig. 1. Blood perfusion of dog's jugular vein. 3 mm. element (*R*). Flow 53 c.c./min. Ordinates: Upper curve, difference in temperature between blood and thermos air in °C. The readings are + when the blood was warmer than the thermos air. Lower curve, junction temperature difference in °C. The readings are + when the downstream junction was warmer than the upstream. Abscissæ: Time in minutes. Lint moistened with warm water was wrapped round the tubing connecting the perfusion bottle to the vein during the interval *A* to *B*.

No readings were taken till perfusion had gone on long enough for the temperature of the apparatus to settle down.

The symbols (*R*) and (*L*) are used in the legends below the figures to show whether the element was put on to the vessel with the leads to the right or to the left side of a person looking downstream.

Results

The following perfusion experiments were done to find out how the differential junctions were affected by rapid changes in the temperature of the blood.

In one series of experiments the temperature of the blood was raised about 1° C. by wrapping a piece of lint moistened in warm water round the tube taking blood from the perfusion bottle to the vein. Readings of the junction temperature difference were taken at minute or half-minute intervals both before and after warming the blood had begun. Fig. 1 is typical of the results with 3, 3·5 and 4 mm. elements. The upper curve shows that the warmed lint applied during time *A* to *B* raised the temperature of the blood entering the vein by about 0·8° C. The lower curve shows that the temperatures of the two junctions were not equally affected, either during or immediately after the procedure. One and a half minutes after putting the lint on at *A*, the downstream junction was 0·08° C. cooler than the upstream.

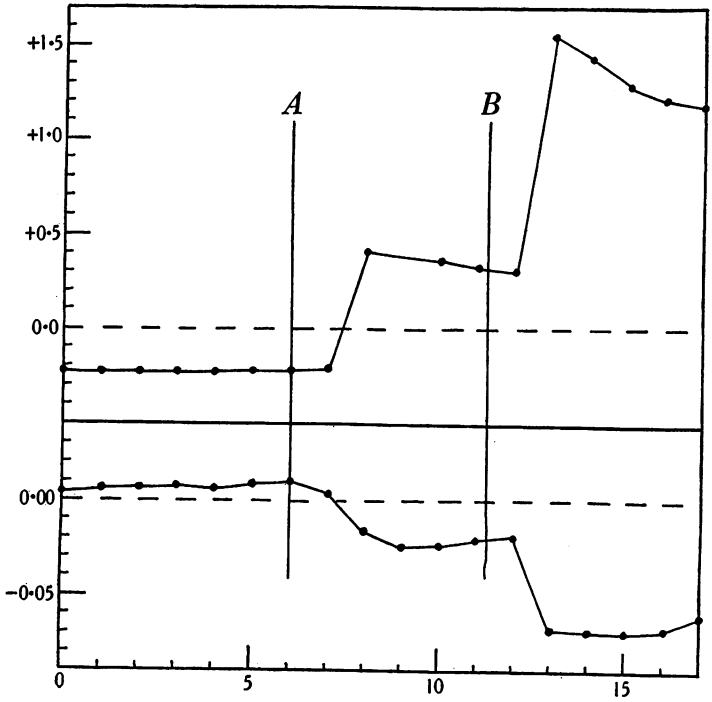

Fig. 2. Blood perfusion of dog's jugular vein. 4 mm. element (*L*). Flow 50 c.c./min. Ordinates: Upper curve, difference in temperature of the outside and inside of the element wall in °C. The readings are + when the inside was warmer than the outside. Lower curve, junction temperature difference in °C. The readings are + when the downstream junction was warmer than the upstream. Abscissæ: Time in minutes. Blood above room temperature was added to that in the perfusion bottle at *A* and again at *B*.

In other experiments the temperature of the blood was altered by adding warmed or cooled blood to the blood in the perfusion bottle. An example from the results with 4, 5, 6 and 7 mm. elements is seen in Fig. 2. Warmed blood was added at *A* and again at *B*. The temperature of the blood entering the vein was raised in two steps by 1·5° C. The downstream junction became 0·07° C. cooler than the upstream, this temperature difference lasted for 4 min.

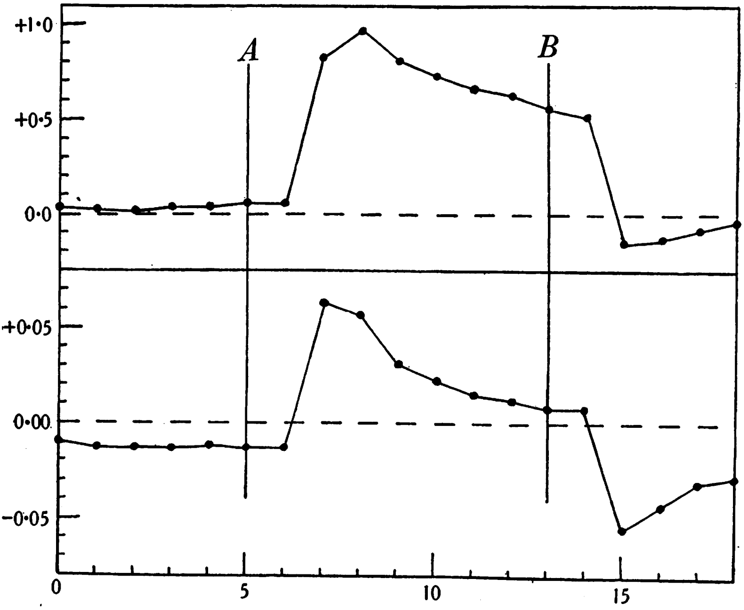

Fig. 3. Saline perfusion of 3 mm. element. No vein. Bare junctions. Ordinates and abscissæ as in Fig. 2. Saline above room temperature was added to that in the perfusion bottle at *A*, saline below room temperature was added at *B*.

We thought the difference in the behaviour of the junctions might be due to differences in the thicknesses of their insulation. Each junction was covered with a thin coat of cellulose varnish. It seemed that elements with bare junctions, sometimes used by Rein *et al.* [1935], might be less unsteady. A 4 mm. element with bare junctions was made and tested. The results were very little better than those obtained with the ordinary elements. (Becquerel & Breschet [1835], Béclard [1861] and Grützner & Heidenhain [1878] found that temperature measurements of the order of 10^{-2} °C. were not reliable if one of the junctions of a couple was in contact with an animal tissue or fluid.)

Although Rein [1931] found that the method gave good results as long as the element was fitted to the vessel with reasonable care we wished to make quite sure that our results were not due to improper application of the element. This was done by eliminating the vein altogether. The top of the element was bridged over with plastic material, and the tube so formed was carefully joined to the perfusion tubing in place of the blood vessel. The junctions were then in direct contact with the blood stream (and also, of course, with the element wall). As the results, shown in Fig. 3, were similar to those shown in Figs. 1 and 2 we thought that the application of the element to the vein, if carefully done, had very little to do with the matter.

A few experiments were done to see if we could predict which of the two junctions would be the more affected by changing the temperature of the blood in a given direction. The junction temperature differences were recorded before and after turning the element through 180°. In three elements the change in the blood temperature always had a bigger effect on the upstream than on the downstream junction. In two elements one of the junctions, which could be identified, seemed to be more sensitive than the other. It did not seem to matter whether it was upstream or downstream, it always followed the blood temperature change more quickly than the other junction.

The perfusion experiments showed that rapid changes of blood temperature of about 1° C. caused junction temperature differences of about 0·07° C.

ANIMAL EXPERIMENTS

In these experiments the behaviour of the differential thermocouple was recorded before and after the intravenous injection of adrenaline in saline. This procedure seemed particularly suitable for the following reasons. Injections of hormones and drugs affecting the circulation are made in many physiological and pharmacological experiments. It is a typical experimental procedure and so is suitable for testing the accuracy of a general method for measuring blood flow. Adrenaline itself is made in the body and is poured into the blood in amounts which vary with the condition of the animal. It seemed likely that adrenaline would affect blood temperature. It seemed likely that it might increase blood temperature, hot blood from the liver and spleen might be added and the circulation through the cold skin might be cut down. It also had the great advantage that the necessary operative interference was very slight, and the animal could not suffer from shock.

Method

The experiments were done under typical conditions. Two kinds of animal, three goats and one dog, were used under chloralose anæsthesia. The operating table had a copper bath filled with warm water. There was an electric stove about 10 ft. from the animal.

The blood vessel to which the element was applied was in the living animal and not in the thermos, otherwise the thermostromuhr technique was as that used in the perfusion experiments. The vessel was prepared and the element carefully put on as directed by Rein [1929*a*]. It was fixed in position with collodion. The edges of the wound were carefully closed, and before any readings were taken sufficient time was allowed for the temperature conditions in the depths of the wound to become normal.

With goats 2 and 3 and with the dog the wound was covered with a thick sheet of cotton wool. The outer surface of the wool was gently warmed by the heat from an electric light bulb. Also the leads to the element were fixed in a clamp some inches from the wound to prevent displacement of the element by accidental movement of the wires.

In these experiments elements were fitted to the vessels, altogether, eleven times. The junction temperature difference was never steadier or smaller than in the perfusion experiments. This is not in keeping with Rein's [1929*b*] finding that temperature conditions in the animal are more uniform than in the thermos. The discrepancy may be due to: (1) The very carefully controlled temperature conditions in our perfusion experiments. Perfusion was started before the thermos was put over the vein. The second thermocouple system then showed the temperature of the perfusion fluid relative to the room air. Warmed or cooled blood was added to that already in the perfusion bottle till the blood flowing into the vein was within less than 0·5° C. of room temperature. The thermos flask was then placed over the vein. Figs. 1, 2 and 3 show that the initial temperature differences between the blood and the thermos air were only 0·1, 0·25 and 0·05° C. respectively. If the blood temperature had been 2 or 3° different from that of the room air, as in Rein's perfusion experiments [1928], the junction temperature differences might have been much greater and less steady. (2) In the dog experiment the element was fitted to the femoral vein. The femoral artery probably touched the element at some point. The temperature of the blood in the two vessels may have been different by several degrees, there may have been a large temperature gradient across the part of the element wall separating the two vessels.

We do not know whether the junctions lay in or near this temperature gradient. As Mr Cowan has pointed out, the position of the junctions relative to the artery probably would have affected the junction temperature difference.

A burette and cannula was attached to the central end of the jugular vein in all experiments. With goats 1 and 2 the adrenaline was injected by hypodermic syringe into the rubber tubing joining the burette to the cannula and was washed into the animal by 5 c.c. of saline from the burette. This had the possible disadvantage that the temperature of the saline was sometimes rather low. With goat 3 and with the dog the adrenaline and the saline were kept warm in the water bath. The necessary amounts, 5 c.c. in all, were drawn into the syringe which was then put back into the water bath. When necessary the syringe was taken out and the adrenaline solution was squirted into the rubber tubing between the screw clip and the cannula, the screw clip was not opened.

In the animals in which the element lay on the carotid the jugular of the opposite side was used for the adrenaline injections. The slight movements of the tubing and cannula caused by inserting the syringe needle had no effect on the junction temperature difference.

Results

The following results are typical of the behaviour of the differential junctions after adrenaline injections.

Fig. 4 was drawn from the observations made on goat 1. The element lay on the carotid artery. Between curves 1 and 2 the element was taken off and carefully replaced. Between curves 2 and 3 the element was taken off, turned through 180°, and replaced. Between curves 3 and 4 the element was taken off again, turned back through 180° to its original position and replaced. Before readings were taken enough time was allowed for the temperature conditions in the wound to become normal. The readings in curve 1 were taken after the element had been in position for over an hour. The adrenaline and saline injections, at *A*, were all followed by changes in the junction temperature difference. In two cases the change amounted to 0·04° C., in the other cases it was less.

Fig. 5 was drawn from the experiment on the dog. The blood pressure at the beginning of curve 1 was 150 mm. Hg. The element was on the femoral vein. In addition to the ordinary differential couple the element had a second couple system with junctions on the inner and outer surfaces of the wall. The upper curves show the temperature difference between the inside and outside of the element. The lower curves show

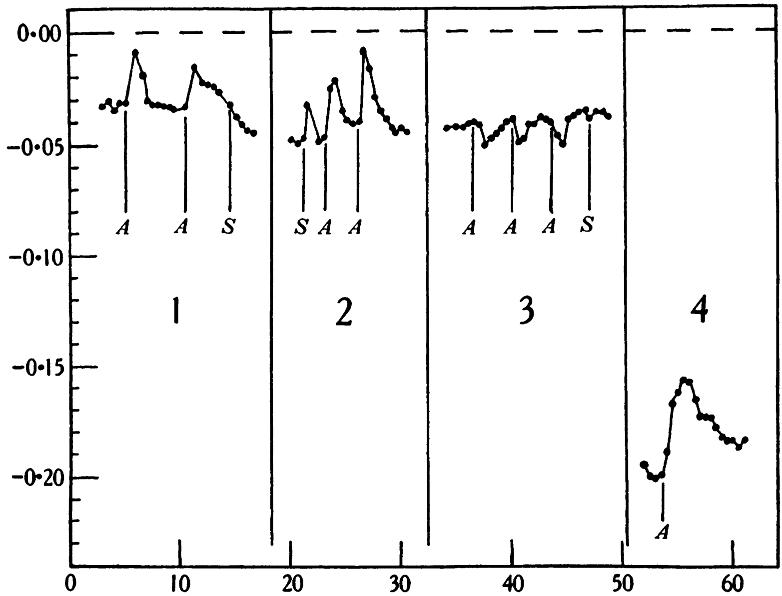

Fig. 4. Goat's right carotid artery. 3 mm. element. The orientation was (*R*), (*R*), (*L*), (*R*) for curves 1, 2, 3 and 4 respectively. Ordinates: junction temperature difference in °C. The readings are + when the downstream junction was warmer than the upstream. Abscissæ: Time in minutes. 5 c.c. intravenous injections of adrenaline in saline at *A*. Reading from left to right the doses were 5, 5, 5, 10, 5, 10, 5, 100μg. Control injections of 5 c.c. saline at *S*.

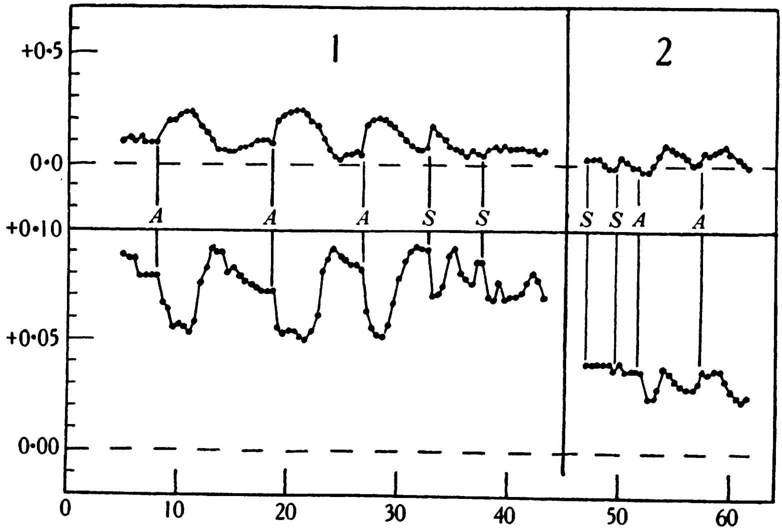

Fig. 5. Dog's right femoral vein. 3 mm. element (*L*). Ordinates and abscissæ as in Fig. 2. Intravenous injections of 50μg. adrenaline in saline at *A*. Control injections of saline only at *S*.

the temperature difference between the ordinary junctions of the element. There was an interval between curves 1 and 2 but the wound was not opened. The adrenaline injections, at A, caused the inner wall of the element to become relatively hotter than the outer, this showed a rise in blood temperature. In the first three injections the difference was 0·15° C. (upper curves). All adrenaline injections except the last changed the junction temperature difference (lower curves). In the first three injections the downstream junction became, relatively to the upstream, 0·04° C. cooler.

Control injections of saline only, at S, are shown in both Figs. 4 and 5. In four out of seven cases they had no effect. In three cases they had an effect which was probably because some adrenaline remaining in the stump of the jugular vein was washed into the circulation.

Sollmann & Gilbert [1938] and others have shown that adrenaline constricts the walls of large arteries. In our experiments adrenaline may have caused trivial movements of the vessel wall near the junctions. This may have had some effect on the junction temperature difference.

These experiments show that a common physiological procedure like the injection of adrenaline in saline, done under quite usual experimental conditions, may change the junction temperature difference by as much as 0·04° C.

THE EFFECT OF RAPID CHANGES IN BLOOD TEMPERATURE ON THE ACCURACY OF THE METHOD

The errors in the flow measurements caused by blood temperature changes can be expressed graphically in a way which readily shows the relation between the various factors concerned.

Rein [1928, 1929 *a*, *b*] has shown that the galvanometer deflexion, G, and the blood flow, V, are related by the expression $GV^{\alpha}=K$, where K is a constant depending on the heating intensity, α is a constant which is less than 1 for most elements. It is never greater than 1. Since the galvanometer deflexion, G, is directly proportional to the junction temperature difference, T, we may write $TV^{\alpha}=k$, and with constant heating intensity $T_{\text{I}}V_{\text{I}}^{\alpha}=T_{\text{II}}V_{\text{II}}^{\alpha}$, where T_{I} and T_{II} are junction temperature differences set up by any two flows V_{I} and V_{II} respectively.

Imagine that at a given moment the actual flow is V_a with junction temperature difference T_a. A change in blood temperature then occurs which alters the temperature of the downstream junction relative to the upstream by t° C. Assuming the actual flow V_a to remain unchanged the junction temperature difference would become T_a+t. The flow would appear to change but actually no change occurred. If V_0 is the apparent flow corresponding to the deflexion T_a+t, then

$$T_a V_a^{\alpha}=(T_a+t)\ V_0^{\alpha}$$

and

$$V_0=\left(\frac{T_a}{T_a+t}\right)^{1/\alpha} V_a. \qquad \ldots\ldots(1)$$

If the blood temperature change warmed the downstream junction the values of t are $+$, the deflexion is increased and the apparent flow V_0 will be less than the actual flow V_a.

Now

$$\text{p.c. error in } V_a=\frac{V_a-V_0}{V_a}\times 100.$$

Substituting the value for V_0 found in equation (1),

$$\text{p.c. error in } V_a=100\left[1-\left(\frac{T_a}{T_a+t}\right)^{1/\alpha}\right]. \qquad \ldots\ldots(2)$$

If the blood temperature change cooled the downstream junction relative to the upstream, the values of t are negative, the deflexion is diminished and the apparent flow V_0 will be greater than the actual flow V_a. The expression then becomes,

$$\text{p.c. error in } V_a=100\left[\left(\frac{T_a}{T_a+t}\right)^{1/\alpha}-1\right]. \qquad \ldots\ldots(3)$$

Inspections of equations (2) and (3) shows that for any given value of α (for any given element) the percentage error in V_a depends on two factors: on T_a the junction temperature difference set up by the heating current, and on t, the junction temperature difference set up by the blood temperature change.

Equations (2) and (3) also show that with any given values of T_a and t the percentage error in V_a is an inverse function of α. The percentage error will be least with elements having an α of 1.

To draw the graph it is necessary to know the limits of T_a and t. The largest values of t in the perfusion experiments were 0·07° C., in the animal experiments they were 0·04° C.; 0 to ±0·07° C. would cover our experiments, and will be taken as the limits, but other experiments and types of element may need different limits.

As will soon be seen, the values of T_a, the junction temperature difference set up by the heating current, are of very great importance to the significance of the percentage error. Unfortunately the ranges of T_a used in thermostromuhr experiments are usually not stated. Indeed Rein [1928, 1929*a*, *b*] and Baldes & Herrick [1931, 1937] seem to hold quite different views about the temperature difference generated between the upstream and downstream junctions by the heating current. To discuss this here would be to risk losing the thread of the present argument. It is safe to say that both Rein and Baldes would probably agree that the junction temperature difference set up by the heating current could not be more than 1° C. For the moment, the limits of T_a will be taken as 0–1·0° C.

Fig. 6 was drawn from equations (2) and (3) taking the limits of T_a and t given above, and taking α as 1.

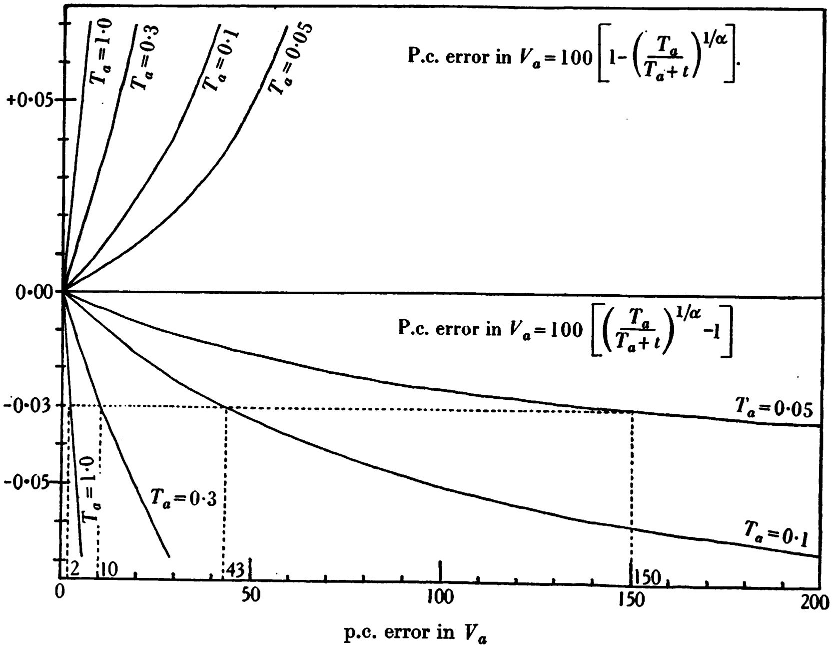

Fig. 6. V_a, actual flow. T_a, junction temperature difference caused by the heating current. t, junction temperature difference caused by change in blood temperature. α, a constant for each element. For further explanation see text.

The values of t were plotted as ordinates, and the percentage error in the flow measurements (in V_a) as abscissæ. The upper curve shows the percentage error when the change in blood temperature causes a rise in the temperature of the downstream junction, the values of t are +, the apparent flow is greater than the actual flow. The lower curve gives the percentage error when the change in blood temperature causes a fall in the temperature of the downstream junction, the values of t are −, the apparent flow is less than the actual flow.

The graphs show the great significance of T_a, the junction temperature difference set up by the heating current; the percentage error is very large with small values of T_a.

The importance of the T_a values is emphasized by taking a figure for t from the adrenaline experiments. In Fig. 5 the changes in blood temperature which followed the first three adrenaline injections changed the temperature of the downstream junction, relatively to the upstream, by about $-0{\cdot}03°$ C. Referring to Fig. 6 and taking the ordinate t is equal to $-0{\cdot}03°$ C. on the lower set of curves the percentage error in the flow measurements after the injections would depend on the value of T_a. The percentage errors would have been 150, 43, 10 and 2 p.c. for values of T_a of 0·05, 0·1, 0·3 and 1·0° C. respectively. In other words, the errors with the low values for T_a would have been so big that the measurements would have been worthless.

The whole question of the size of the error depends on the junction temperature difference set up by the heating current.

Both Rein [1928, 1929*a*, *b*] and Herrick & Baldes [1931] limit the amount of heat generated in each cubic centimetre of blood flowing through the element to 0·1 cal. Rein and Baldes disagree about the extent to which this heat would raise the temperature of the downstream junction, T_a. Rein [1929*a*] found that the rise in temperature caused by the heating current was uniform over a cross-section of the vessel at the level of the downstream junction. He did not describe the method. Sometimes there was a slight loss of heat through the element wall and along the constantan wire towards the cooler upstream junction. If this is true, if the heating current heats the blood uniformly near the downstream junction, then the maximum heating current, 0·1 cal. per c.c. of blood, would raise the temperature of the blood by 0·1° C. and the rise in temperature at the downstream junction, T_a, could not be more than 0·1° C. Fig. 6 shows that if the values of T_a are 0·1° C. or less changes in blood temperature may cause very large errors in the flow measurements.

Herrick & Baldes [1931] do not agree that the blood is uniformly heated. They say: "The fact that the galvanometer always records a temperature difference along the vessel wall many times greater than can exist in uniformly heated blood fails to lend support to the theory." If this is right the junction temperature difference, T_a, due to passing 0·1 cal. into each cubic centimetre of blood, must be many times more than 0·1° C. Fig. 6 shows then when the values of T_a are much more than 0·1° C. the errors due to blood temperature changes are much smaller.

We are very much indebted to Mr Cowan for a suggestion which enabled us to test these views.

We had done over sixty perfusion experiments to calibrate our elements. We had a series of readings for each element. For each reading the corresponding values of 1, 2 and 3 given below were known and the values of 4 and of 5 were calculated from them:

1. The flow.
2. The junction temperature difference T_a.
3. The heating intensity.
4. The rise in the temperature of the blood assuming it to have been uniformly heated. Obtained from 1 and 3.
5. X, the ratio of 2 to 4.

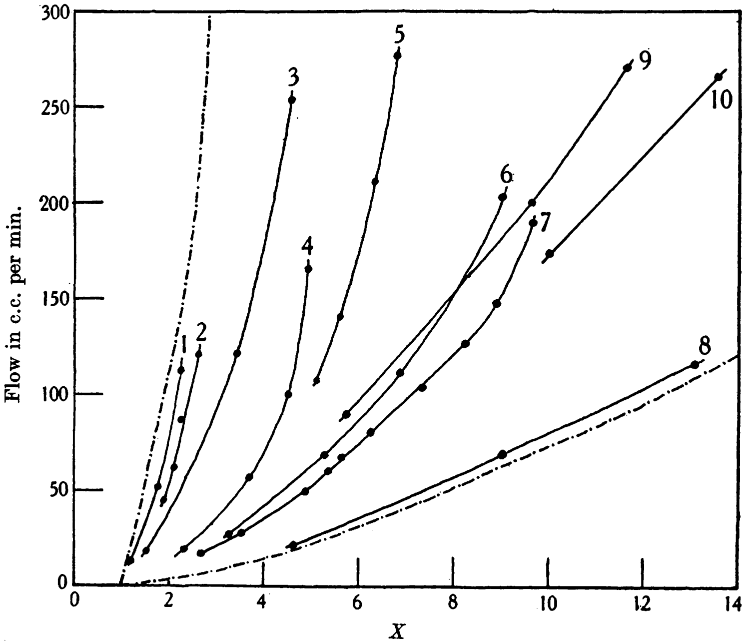

Fig. 7. The sizes and types of element were as follows: Curves 1, 6 and 7, 3·5 mm.; 8 and 10, 4·5 mm.; 9, 5·5 mm.; 3, 3·5 mm., no vein; 4, 3 mm., Baldes A.C.; 2, 4 mm., Baldes A.C.; 5, 5 mm., Baldes A.C. For further explanation see text.

The ratio X showed how much hotter the downstream junction was than it should have been on the assumption that the blood had been uniformly heated. When the ratio was 1 the blood could have been uniformly heated.

Fig. 7 shows the results. The flow is plotted against the ratio X. Each of the curves was drawn from the readings of a different calibration experiment. The sizes and types of element used are given below the figure.

All the curves lie inside the dotted lines. As the flows get smaller the limits converge and approach the value $X=1$. Rein's finding, that the blood is uniformly heated, may be nearly true for very low flows, lower than those we used. For the normal range of flows the values of X are greater than 1. For flows of 100 c.c./min. the vessel wall at the downstream junction was 2–12 times hotter than it should have been on the assumption that the blood was uniformly heated. For the range of flows we used in our calibration experiments our results support Baldes.

As the rise in the temperature of the vessel wall is an inverse function of the rate of blood flow the greatest galvanometer deflexions and T_a values are those with the slowest flows. Referring to Fig. 7 the lowest flows in our calibrations were about 25–50 c.c./min. The corresponding values of X are from 1·5 to 8. That is, the largest values of T_a, with a heating current generating not more than 0·1 cal./c.c. of blood, would not have been more than 0·8° C. The values of T_a for thermostromuhr experiments with the types of element we have used probably lie within the limits of 0 to 0·8° C.

The above may be summarized as follows:

(1) If the blood is uniformly heated the maximum junction temperature difference set up by the heating current will be about 0·1° C. Most readings will be taken with half or three-quarter full scale deflexions of 0·05 to 0·075° C. junction temperature difference. The errors caused by the changes in blood temperature in our adrenaline and perfusion experiments would sometimes have been more than 100 p.c.

(2) If, as we find, the blood is not uniformly heated, and the heat is concentrated near the vessel wall, the maximum junction temperature difference set up by the heating current will be between 0·1 and 0·8° C. The actual limits of T_a used in any given thermostromuhr experiment are usually unknown because the thermocouple circuit is not usually standardized and the galvanometer deflexions cannot be converted into degrees centigrade. The errors for our experiments would usually have been less than 100 p.c.

DISCUSSION

Kramer [1936] tested the accuracy of the thermostromuhr. In one series of experiments he measured the percentage change in the flow in the femoral artery with the thermostromuhr and by a photometric method. Both methods were used simultaneously. Both showed that when the animal breathed 3·95 p.c. oxygen the flow increased by about 80 p.c. Both gave the same time relations for the changes in flow.

In other experiments Kramer measured the flow in the femoral artery by the photometric method only. Intravenous injection of 10 μg. of adrenaline caused changes in flow similar to those Rein had found with the thermostromuhr.

These experiments prove the accuracy of the thermostromuhr in the above experiments.

We do not think that this is a proof for thermostromuhr experiments in general, because:

(1) Other physiological and pharmacological procedures may cause much greater changes in blood temperature. For example, perhaps muscular activity.

(2) For any given procedure the blood temperature changes are probably different in arteries and veins.

(3) For any given procedure, and any given blood vessel, the blood temperature changes may vary with the temperature of the animal's surroundings.

(4) For given blood temperature changes the errors depend on the junction temperature difference set up by the heating current. If the junction temperature difference is less than 0·1° C. the errors will be very much greater than if the junction temperature difference is, say, 0·5° C.

(5) The Rein "Form III", Baldes A.C. [1933], Baldes D.C. [1937] and Schmidt & Walker [1935] elements are so different that a given blood temperature change will probably set up different junction temperature differences in these elements.

We believe that all thermostromuhr measurements should be carefully controlled to avoid errors due to blood temperature changes. Such errors are not likely to arise so long as the circulation is in a comparatively steady state. They are more likely to occur when rapid vascular changes are going on, when there is a quick redistribution of the blood, and when parts of the body are undergoing rapid changes in temperature due to activity or changes in surrounding temperature.

It would be quite easy to get an idea of the error likely to affect the flow measurements in an experiment by:

(1) Standardization of the thermocouple circuit so that the galvanometer deflexions could be turned into degrees centigrade junction temperature difference. The junction temperature difference T_a set up by the heating current would then be known.

(2) Doing the experiment a number of times, without the heating current, to find the limits of t, the junction temperature difference set up by the blood temperature changes.

(3) Reference to graphs, like Fig. 6, to find the percentage error corresponding to the values of T_a and t.

A statement of the values of T_a and t might be useful to others doing the same kind of experiment.

SUMMARY

1. Physiological changes in blood temperature may affect the accuracy of the thermostromuhr method.

2. The significance of the error depends on several factors and especially on the junction temperature difference caused by the heating current.

3. The error in measuring the flow through the femoral vein after adrenaline would have been approximately 150, 43, 10 and 2 p.c. for junction temperature differences of 0·05, 0·1, 0·3 and 1·0° C. respectively.

4. A method is given for finding the significance of the error.

The authors collaborated in the earlier and most difficult stages of the work. W. M. Loughridge was unfortunately obliged to leave before the animal experiments were done.

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