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THE EFFECT OF LOCAL TEMPERATURE ON FLUID LOSS IN THERMAL BURNS

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The rapid outpouring of plasma from the blood stream into the affected area is one of the most striking and important features during the first 48 hr. after thermal injury. The loss of fluid may be sufficient to cause shock and even death from circulatory collapse, if the area of the burn is sufficiently great, since the compensatory withdrawal of fluid from the undamaged tissues, although considerable, is not sufficient to prevent a fall in plasma volume during the early period of rapid oedema formation. This upset in the water balance of the body, resulting from the local damage to the capillaries, is greatest during the first 18 hr., and usually ceases at about 48 hr. The literature on this subject of fluid loss after thermal burns has in recent years been reviewed by Harkins (1938, 1942, 1944), and will not be repeated here.

The main treatment of thermal burns, as far as the plasma loss and shock are concerned, is replacement by plasma or serum transfusions. These transfusions will probably increase the local oedema but, if given repeatedly, generally restore the plasma volume. More recently attempts have been made in experimental animals and in man to lessen the degree of plasma loss by applying pressure to the injured part (Barnes & Trueta, 1941; Glenn, Gilbert & Drinker, 1943; Rossiter, 1944; Cameron, Allen, Coles & Rutland, 1945; Cope & Rhinelander, 1943). This pressure-bandaging increases the effective tissue tension and so tends to prevent the escape of plasma from the injured capillaries.

The experiments to be described below have also been designed to show whether the production of oedema can be lessened by keeping the affected areas cold as compared with keeping similarly affected areas warm. It was thought that the amount of oedema formation would depend upon the quantity of blood flowing through the damaged capillaries. Usually, in the treatment of burns, the affected part is kept warm with a resultant good blood flow. By keeping the local area cold, it was hoped to decrease the blood flow and so lessen the degree of fluid loss, especially in the early stages when the outpouring of plasma is so rapid.

METHODS

General. Rabbits, dogs and goats have been used in this investigation. In all animals the legs have been the part burned. Before scalding, the legs in all animals were clipped.

Rabbits were anaesthetized with nembutal intravenously, and the hindlegs (one or both as stated) scalded in a beaker of water at 75° C. for 45 sec. The legs were always immersed to approximately the same depth, viz. just below the knee joint. This has been the standard burn for rabbits used throughout this investigation. Except in those cases where stated, the rabbits, after burning, were allowed to recover from the anaesthetic, which usually took 1–2 hr. When they had recovered they were given greens to eat and water to drink.

In the various experiments the hindlegs were kept at a constant temperature after burning, 0, 37, or 45° C., for periods of 2, 6, 12, 24 or 48 hr. This was done as follows: A 6 in. wide plaster of Paris bandage was placed around the posterior part of the rabbit's abdomen. This prevented the rabbit from flexing its hip joint, and as a rabbit does not flex its knee joint with the hip joint in extension the two hindlegs were kept fairly straight and not flexed under the abdomen. The rabbit was then put in a rabbit box with a hole in the posterior end through which protruded the hind part of the animal. After recovery from the anaesthetic, the rabbit remained in the box quite happily with its hindlegs hanging in a water-bath kept at the required constant temperature. Each leg was placed in a cylindrical rubber bag after burning, so that the legs were kept reasonably dry.

Goats were anaesthetized with nembutal intravenously, and the legs burned by standing them in drums containing water at 85° C. for 2½ min. They recovered from the anaesthetic in about ½ hr. The legs were kept at the required temperature by placing them in drums of water at that temperature. The legs on one side of the goat were kept in ice-water and those on the other side at room temperature or in water at 37° C.

Dogs were anaesthetized with nembutal intravenously and kept under the anaesthetic throughout the experiment. The paws (fore or hind) of the dog were scalded in water at 90° C. for 2 min. or 80° C. for 1½ min. Dogs have been used for the measurement of the lymph flow and blood flow in the burned paw when kept at various temperatures afterwards.

In the investigation of the lymph drainage of the burned area, the main lymph duct of the foreleg was cannulated just above the paw, and in the hindleg one of the lymph ducts running alongside the external saphenous vein was cannulated, the other being ligatured. Dry heparin was placed in the cannula at intervals to prevent coagulation. Samples of lymph were collected at various times before and after burning, as described below.

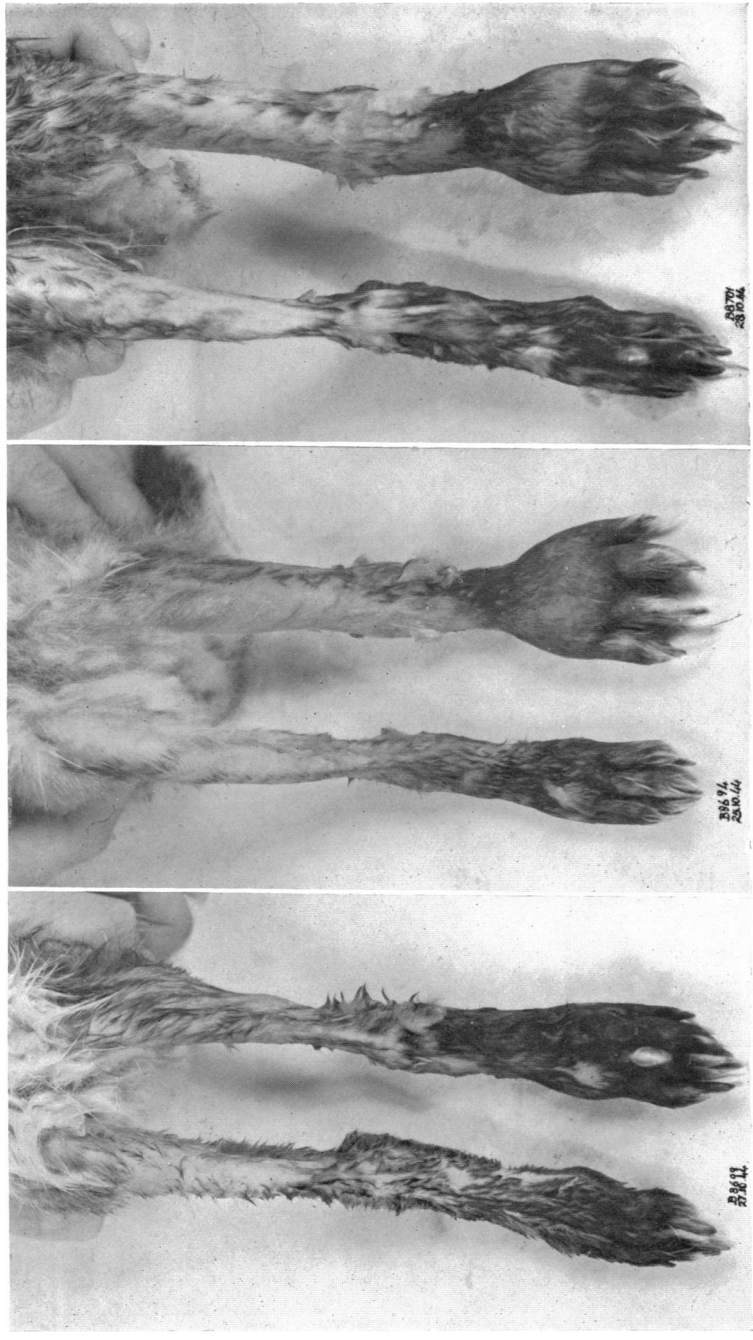
The blood flow of the forepaw in the dog was estimated simply by inserting a Y-shaped cannula in the course of the large vein draining the foreleg just above the paw. The blood could be allowed to circulate normally or, by clipping the proximal end of the vein and unclipping the side tube, the blood flowed along the latter into a 25 c.c. pipette. The time taken to fill the pipette was noted and the rate of blood flow estimated. The blood was then reintroduced into the circulation. In these experiments the dog was supported in the prone position on a frame with the forelegs hanging down. The pipettes were sloped at an angle roughly parallel to the forelegs and were fixed in position. The pressure of the column of blood in the pipette was therefore kept at a minimum and the same throughout the experiment. The blood was made incoagulable by the intravenous injection of heparin, 300 units per kg., followed 1½ hr. later and then hourly by 150 units per kg.

Analytical methods. (*a*) Haemoglobin was estimated by the Haldane haemoglobinometer.

(*b*) Plasma and lymph protein concentrations were determined by micro-Kjeldahl digestion and Nesslerization.

(*c*) Plasma non-protein nitrogen (N.P.N.) was determined by precipitation of the proteins with trichloroacetic acid, micro-Kjeldahl digestion and Nesslerization.

(*d*) Body temperature was measured by clinical thermometer. The temperature of the rabbits was recorded in the mouth between the cheek and the gums, since the rectal temperature might



The general appearance of the effects of local temperature on the amount of oedema formation in the scalded hindlegs of rabbits.
For explanation see text (p. 323).

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be affected by the temperature of the water-bath into which the hindlegs were immersed. In ten normal rabbits it was shown that the mouth temperature was consistently a little lower than the rectal temperature, 0·5° F. on the average. Since rabbits do not breathe through the mouth, the mouth temperature should give a good indication of the general body temperature.

(*e*) Blood pressure was measured in rabbits by the Grant-Rothschild method (Grant & Rothschild, 1934). Great care was taken to have the rabbit quiet and the ear artery completely dilated by warming. Each determination of the blood pressure is the mean of ten readings.

(*f*) The oxygen content of the blood was determined with the van Slyke manometric apparatus. For these estimations the blood was withdrawn under liquid paraffin, and the analyses begun within the next 3 hr.

In the rabbits, all blood samples were taken from the ear vein.

Results

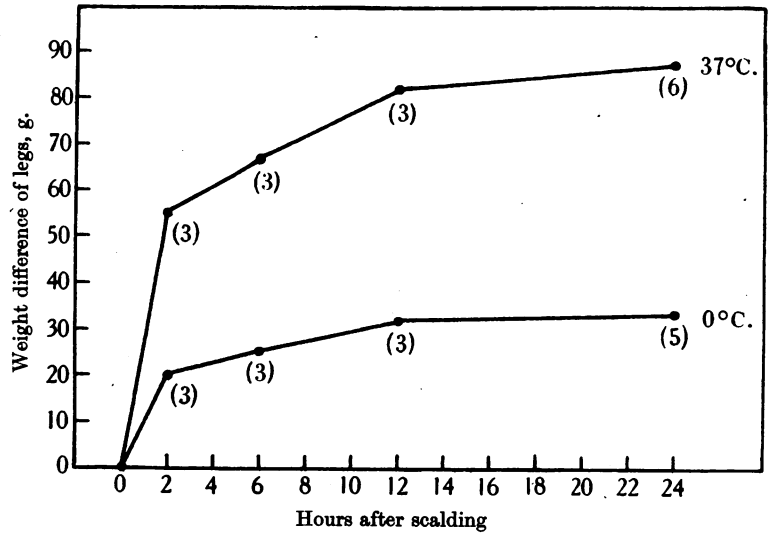
The effect of local temperature on the amount of oedema formation after scalding

The general appearance of the hindlegs of rabbits, scalded at 75° C. for 45 sec., and then kept cold (in ice-water) or warm (in a water-bath at 37° C.) can be seen in Pl. 1. In rabbit (*a*) the left hindleg has been scalded and both legs then kept in water at 0° C. for 2 hr.; in rabbit (*b*) the left hindleg has been scalded and both legs kept in water at 37° C. for 2 hr.; in rabbit (*c*) both hindlegs have been scalded, the right leg then being kept in ice-water and the left leg in water at 37° C. for 2 hr. These photographs are typical of a large series of experiments. In every case the scalded leg kept in ice-water shows little oedema formation, whereas the scalded leg kept warm at 37° C. shows immense swelling.

The actual amount of oedema formation has been measured by scalding one hindleg and then keeping both hindlegs at 0° C. or at 37° C. for the required time, when the animal was killed, the two hindlegs carefully dissected at the hip joint and weighed. The difference between the weights of the two legs has been taken as a measure of the oedema formation. Since no oozing occurs in animals, this method should give a good indication of the plasma loss from the circulation. A slight error is probably introduced by the withdrawal of tissue fluid from the undamaged tissues into the blood stream in an endeavour to compensate for the fall in plasma volume. Some of this tissue fluid will come from the undamaged leg below the knee, corresponding to the damaged counterpart, making the undamaged leg lighter and, therefore, increasing the difference in weights. The weight of the leg below the knee joint, however, is only about 80 g. in a 2300 g. rabbit, so the actual decrease in weight of the normal leg must be insignificant.

Eight groups of rabbits have been used in this experiment. In four groups the legs were kept at 0° C. after one leg had been scalded, one group for 2 hr., one for 6 hr., one for 12 hr. and one for 24 hr. Similarly, in four other groups, the legs were kept at 37° C. The average body weight in each group was 2·3 kg., and each individual rabbit was approximately 2·3 kg. At the end of the

required time for any group, the rabbits were killed and the hindlegs dissected and weighed. The average results are shown graphically in Text-fig. 1. It can clearly be seen that very much less plasma loss occurs when the burned limb is kept cool than when it is kept warm, and that in both conditions the outpouring of plasma is most rapid in the first 2 hr. and then becomes gradually slower. The plasma loss in the legs kept warm would probably continue at a greater rate but for the fact that the burned skin cannot stretch any more, and the increased tissue tension forces the oedema fluid up the leg above the upper limit of the burn. In the legs kept cold the outpouring of fluid, even



Text-fig. 1. The amount of oedema fluid in one hindleg, of the rabbit, scalded in water at 75° C. for 45 sec., when the local temperature is 0 or 37° C. The figures in brackets represent the number of rabbits in each group.

after 24 hr., is not great enough to cause tracking up the leg to the undamaged area of the thigh. Expressed as percentage of the body weight, the average loss of plasma from the one burned leg kept cold for 2, 6, 12 and 24 hr. is 0·9, 1·1, 1·3, and 1·4 respectively, whereas that from the one burned leg kept warm is 2·5, 2·9, 3·6 and 3·8 respectively. As the normal plasma volume of the rabbit is approximately 5 % of the body weight (Courtice, 1943), the plasma loss from the warm leg would cause death but for the considerable withdrawal of tissue fluid from the normal tissues into the blood stream. The degree of haemoconcentration will be considered below.

In a further series of six rabbits, both hindlegs were scalded, and one leg was kept at 0° C. and the other at 37° C. for 2 hr. The average weight of the six rabbits was 2·3 kg., and the average difference of weight of the two legs

32 g., which corresponds closely with the difference in weights of the warm and cold groups at 2 hr. in the experiments represented in Text-fig. 1.

These experiments, therefore, show that if the scalded limb is kept cool immediately after scalding, the loss of plasma is very much less than when the limb is kept warm. Further experiments show that if the limb has been warmed for 2 hr. after scalding, the process of oedema formation can be slowed by then keeping the limb cool. One hindleg of each of four rabbits, each weighing 2·3 kg., was scalded. Both legs were then kept at 37° C. for 2 hr. and then in ice-water for 22 hr. The average difference in weight was 44 g. at the end of the experiment. This compares with an average difference of 87 g. had the legs been kept at 37° C. for the 24 hr. (cf. Text-fig. 1). Further evidence of the effect of cold treatment after 2 hr. at 37° C. will be given later.

The effects of local temperature have also been determined in a small series of goats. In the first experiment, both forelegs and both hindlegs of two goats anaesthetized with nembutal were immersed in drums of water at 85° C. for 2½ min. to a depth just below the knee joint and below the elbow joint. In each animal the two comparable legs were immersed in the same drum at the same time to approximately the same depth. After scalding, the goat was stood with one foreleg and one hindleg in drums of ice-water, and the other two legs at room temperature. The goat recovered from the anaesthetic in about ½ hr. and then stood unsupported. At the end of 6 hr. the goats were killed and the legs carefully dissected at the knee or elbow joints and weighed. The results are given in Table 1.

In two other goats the hindlegs only were scalded as previously. After scalding, one hindleg was kept in ice-water and the other in a drum of water, kept at 37° C. by a heating element and thermostat. The goats were allowed to recover from the anaesthetic. After 6 hr. the goats were killed and the legs carefully dissected and weighed. The results are given in Table 1.

TABLE 1. The effect of local temperature on the amount of oedema in legs of goats scalded at 85° C. for 2½ min. Killed 6 hr. after scalding

Goat	Weight kg.	Hindleg wt. in g.			Foreleg wt. in g.		
		0° C.	Room temp.	Diff.	0° C.	Room temp.	Diff.
1	28	772	865	93	624	688	64
2	27	800	934	134	637	684	47
		0° C.	37° C.	Diff.			
3	25	895	1027	132			
4	27	855	1067	212			

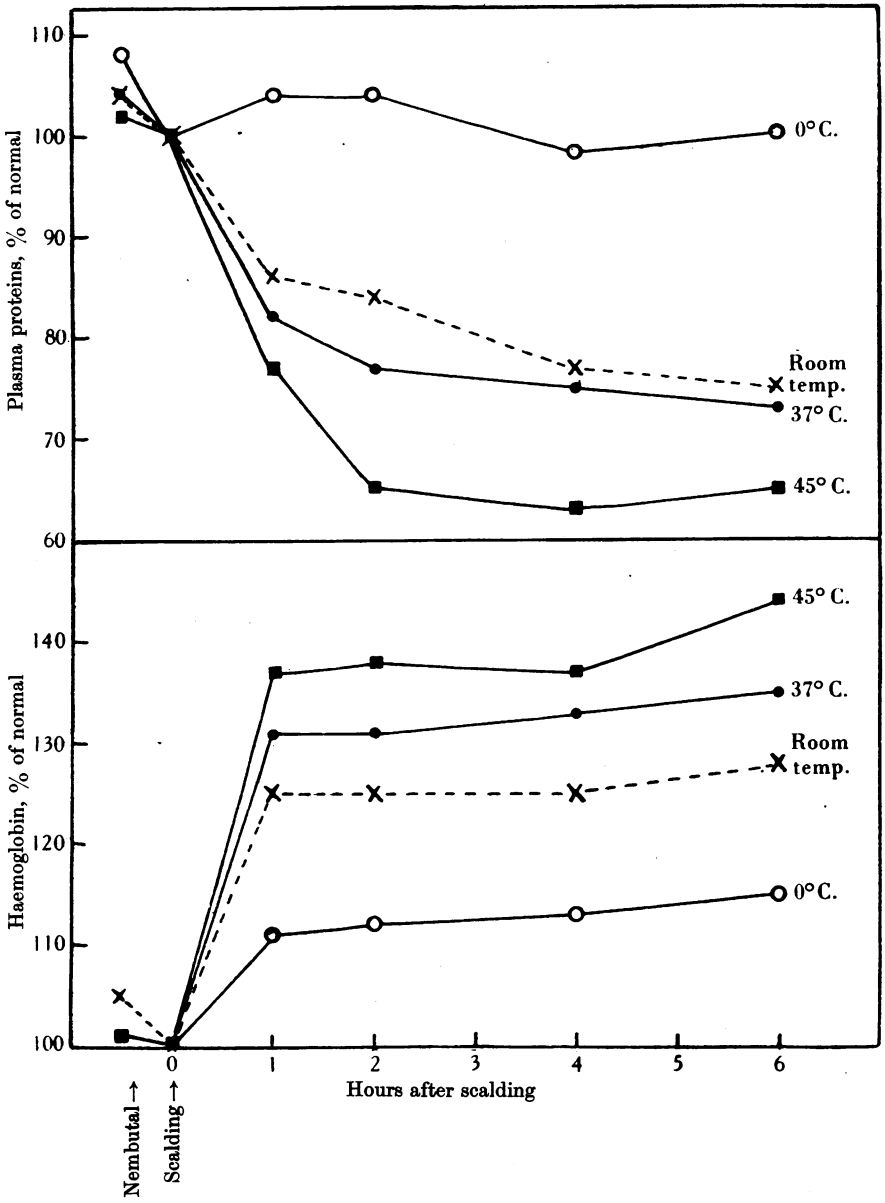
All burned legs showed oedema, but those kept in ice-water were much less oedematous than those kept at room temperature or 37° C. as the figures in Table 1 indicate. In the goat the lower part of the legs have little flesh, so the skin covers the bones fairly tightly. There is thus not room for much

oedema formation, the skin acting as a tight plaster bandage. Even so, there is a considerable difference in the oedema formation, which varies with the local temperature.

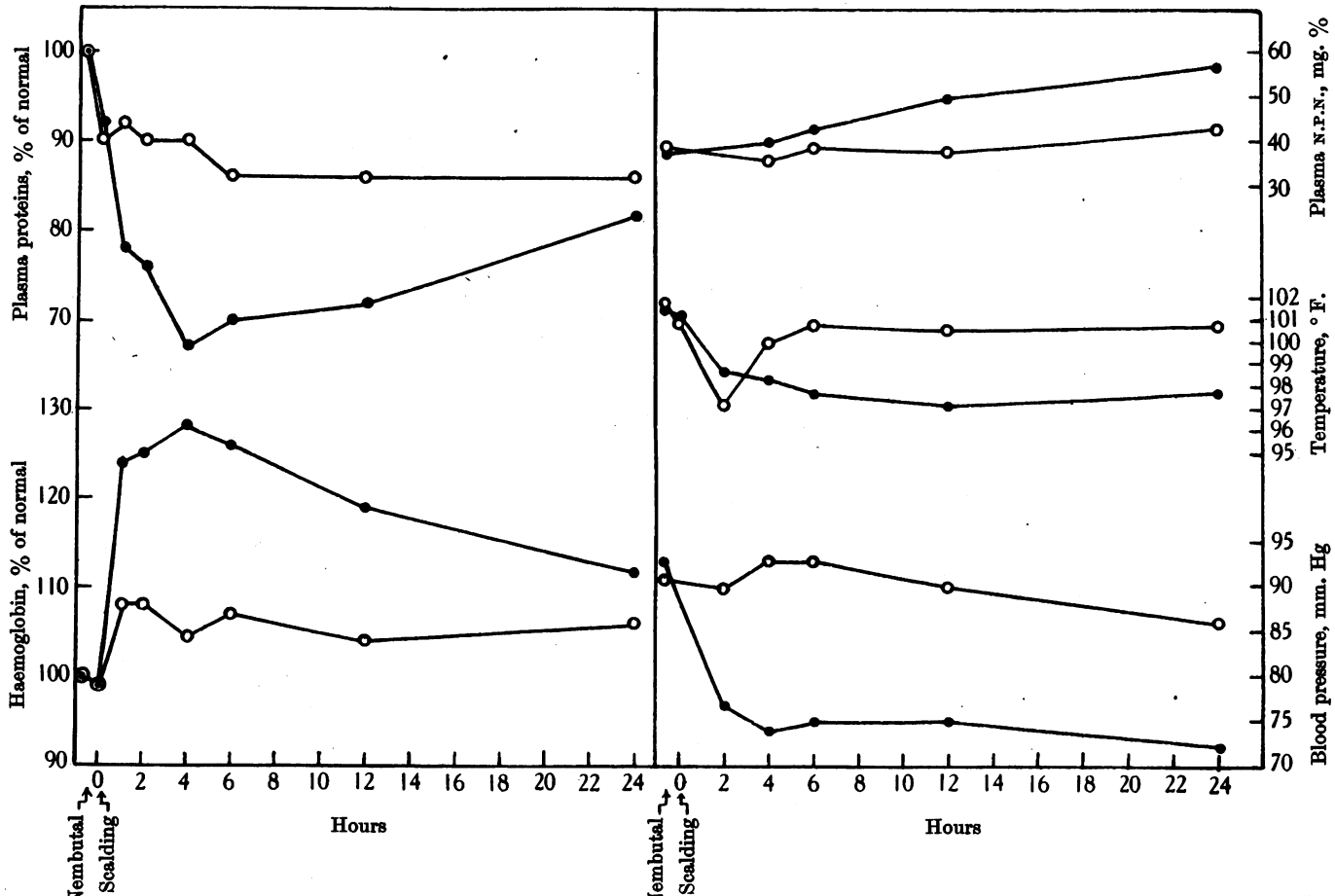
Effects of plasma loss on haemoconcentration and plasma proteins

Two series of experiments were performed in which the haemoglobin and the plasma-protein concentration were determined before and at intervals after burning. In the first series the rabbits were kept anaesthetized by repeated small injections of nembutal for 6 hr. after burning, when the experiment terminated. Both hindlegs were scalded and were then kept in a water-bath at 0, 37 or 45° C. or kept at room temperature not in a water-bath. Blood samples were taken before nembutal, after nembutal before burning, and 1, 2, 4 and 6 hr. after burning. Five animals were used in each group except the 45° C. group in which seven were used. The average results for each group are shown in Text-fig. 2. In this diagram the haemoglobin and plasma-protein concentration are expressed as a percentage of the normal value just before burning. It can be seen that the warmer the injured legs are kept, the greater the haemoconcentration and the less the plasma protein concentration. This is due to the more rapid outpouring of plasma and the greater withdrawal of tissue fluid back into the circulation, the warmer the local temperature. In the group of rabbits kept at 45° C., five animals out of seven died in 2–6 hr., so the 4 hr. point is the mean of only three animals and the 6 hr. point the mean of only two animals. It seems that in those that died, the loss of plasma was too great and too rapid to be compatible with life.

In the second series of experiments, the rabbits were allowed to recover after burning, and were examined for 24 hr. They were given cabbage to eat and water to drink. Besides the haemoglobin, plasma protein and N.P.N. concentration, the mouth temperature and blood pressure were recorded. Both hindlegs were scalded in two groups of animals. One group was then kept with the hindlegs in a bath at 0° C. and the other group in a bath at 37° C. The average results of each group of four animals are shown in Text-fig. 3. Three further animals in each group were used with similar results for the haemoglobin and plasma-protein concentration, but in these animals the blood pressure and mouth temperature were not observed. The results of the determinations on the group of rabbits whose legs have been kept at 37° C. show a rapid rise in the haemoglobin and fall in plasma-protein concentration with the rapid onset of oedema (cf. Text-fig. 1). The maximum rise in haemoglobin and fall in plasma protein occurs about 4–6 hr. after scalding. From the single burnt leg in the experiments depicted in Text-fig. 1, it would appear that the amount of fluid lost into both legs should be greater than the original plasma volume. The withdrawal of tissue fluid into the blood stream, however, prevents the haemoglobin from rising above about 130% and dilutes the plasma

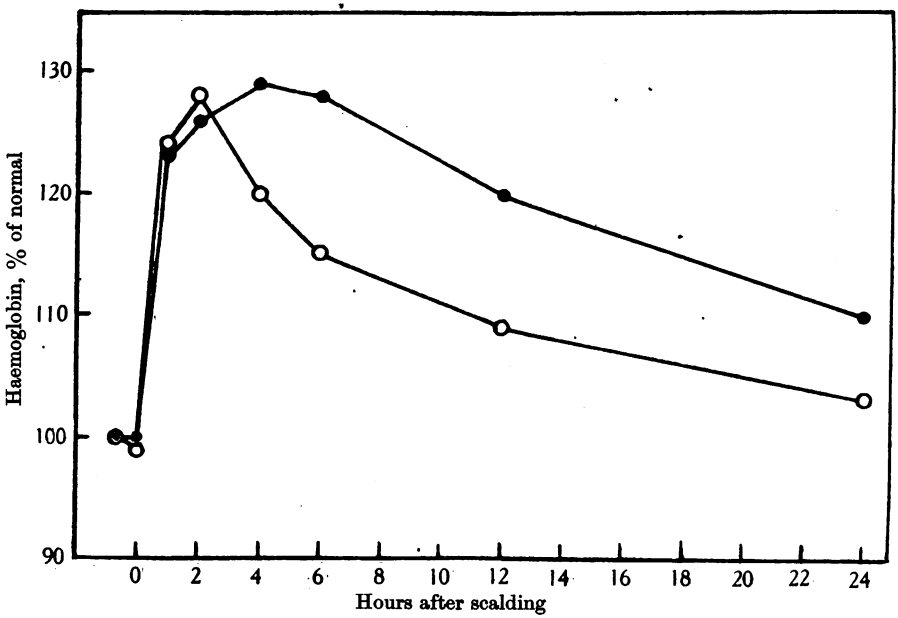


Text-fig. 2. The haemoglobin and the plasma-protein concentration represented as a percentage of the pre-scalding level when both hindlegs of rabbits were scalded. Each graph shows the average results from a group of five animals.



Text-fig. 3. The haemoglobin, plasma-protein concentration, blood pressure, mouth temperature and plasma non-protein nitrogen (N.P.N.) in rabbits. At zero, both hindlegs were scalded and the rabbits were allowed to recover from the nembutal. ●——● Local temp. 37° C. Mean of four animals. o——o Local temp. 0° C. Mean of four animals.

proteins to about 70% of their pre-burning level. After 6 hr., plasma continues to be lost locally, as seen in Text-fig. 1, but the rate of withdrawal of fluid into the circulation overtakes the outpouring of plasma into the damaged tissues, so that the haemoglobin percentage falls. The plasma-protein level also rises, due probably to regeneration or mobilization of new protein. Compared with these changes in experiments at 37° C., the changes in rabbits whose scalded legs are kept cool are very slight. The N.P.N. in the 'warm' experiments also rises during the first 24 hr., as it does in all cases of anhydraemia no matter



Text-fig. 4. Haemoglobin in two groups of rabbits after scalding both hindlegs. •——• Local temp. 37° C. for 24 hr. Mean of seven animals. o——o Local temp. 37° C. for 2 hr. and 0° C. for 22 hr. Mean of four animals.

how it is produced, whereas in the 'cold' experiments with very little anhydraemia there is practically no rise in N.P.N. The blood pressure likewise shows practically no change in the 'cold' experiments, but a considerable fall in the 'warm' experiments, with haemoconcentration. The mouth temperature in all animals burned, whether they showed haemoconcentration or not (see later experiments), fell considerably during the first 2 hr. after burning. This seems to be a nervous reaction causing an early and substantial vaso-constriction of the peripheral vessels, for during this period it is generally difficult to dilate the ear vessels by warmth, even though the blood pressure is not low. In the animals whose legs are kept cold, however, the mouth temperature then rises and remains fairly constant at nearly normal level. In the animals with legs kept warm, the mouth temperature continues to fall. This is probably due to

vaso-constriction of the peripheral vessels to compensate for the fall in plasma volume.

These experiments show that if the burned area is kept cold immediately after the injury, the blood and circulatory changes can be greatly lessened as compared with those in similarly burned animals with the legs kept warm.

It has already been seen that if the burned area is kept at 37° C. for 2 hr. and then at 0° C. for 22 hr. the oedema is much less than if the legs were kept at 37° C. for 24 hr. The effect of cold in slowing down oedema formation after 2 hr. at 37° C. can also be shown by estimating the degree of haemoconcentration. Text-fig. 4 shows the average haemoglobin changes in a group of seven rabbits with both hindlegs scalded and kept at 37° C. for 24 hr. and of a group of four rabbits similarly burned, with the hindlegs kept at 37° C. for 2 hr. and then at 0° C. for 22 hr. The haemoconcentration in both groups is almost identical in the first 2 hr. The withdrawal of tissue fluid of the second group when the legs are placed in ice-water continues as in the first group, but the outpouring of plasma into the damaged tissues is slowed, with a resultant sharp downward trend in the curve. Thus, even if cold is applied as late as 2 hr. after burning, the outpouring of plasma can be definitely slowed down.

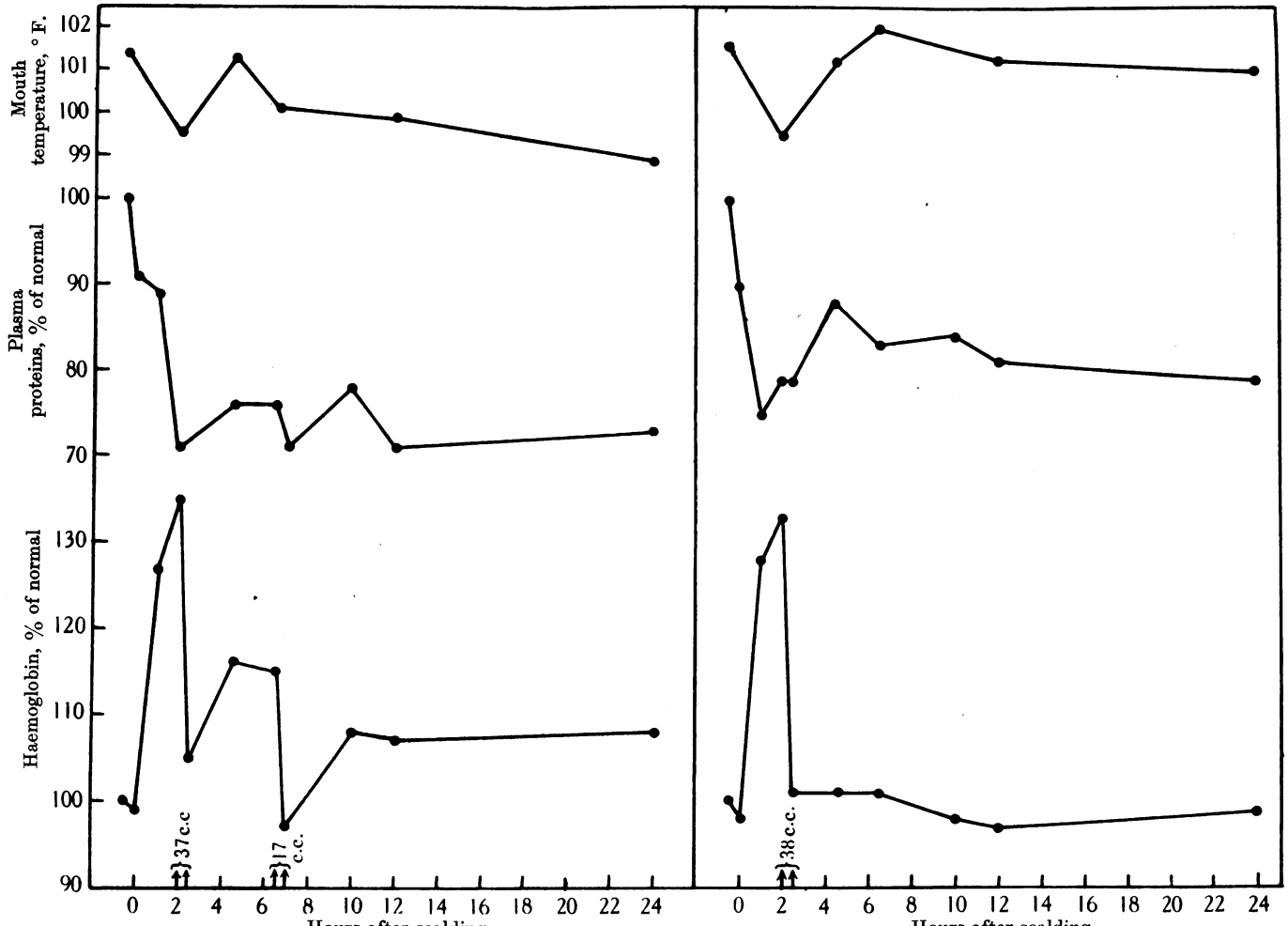
The effects of transfusion of plasma and serum

In these experiments both hindlegs of rabbits have been burned, and kept at 37° C. for 2 hr. At 2 hr. one group has been transferred to ice-water and transfused, while the legs of the other group have remained in the water-bath at 37° C. and the rabbits transfused. Both plasma and serum (rabbit) have been used in these transfusions.

Text-fig. 5 shows the effects of the plasma transfusions. Two hours after burning, the blood of both groups of rabbits had concentrated to about the same extent. Plasma transfusion reduced the haemoglobin to approximately the pre-burning level. The rabbits whose legs were kept warm then rapidly lost more plasma and the blood concentrated again. A further transfusion at 6 hr. again brought the haemoglobin down to normal, but further outpouring of plasma caused haemoconcentration once more. With the group of rabbits transferred to the cold water-bath, the transfusion restored the haemoglobin to normal, and this level was maintained throughout the 24 hr. After the initial fall, the plasma-protein concentration was maintained at a higher level in the cold group than in the warm group. The mouth temperature returned to normal in the cold group and remained normal after transfusion, whereas in the warm group the temperature rose after transfusion and then fell again.

Similar results have been obtained after serum transfusion.

The serum reduced the haemoglobin and increased the plasma-protein concentration and mouth temperature in the cold group, and these normal values were maintained for 24 hr. In the warm group the beneficial effect of



Text-fig. 5. Effects of plasma transfusion in rabbits after scalding both hindlegs. Left: local temp. 37° C. for 24 hr. Mean of three animals. Right: local temp. 37° C. for 2 hr. and then 0° C. for 22 hr. Mean of three animals.

the serum was transient, and as further fluid was lost into the damaged tissues, the haemoglobin rose and the plasma-protein concentration and mouth temperature fell.

These transfusion experiments show that if the affected limbs are kept cool, less plasma or serum is required to maintain the blood and circulation at a normal level, which indicates that much less leakage occurs if the burned area is kept cool than if it is kept warm.

The effects of local temperature on lymph flow from scalded paws of dogs

Lymph flow in normal legs. In these experiments the lymph duct in the hindleg or foreleg of dogs, anaesthetized with nembutal, was cannulated. Lymph was collected by massage at regular intervals, since there is no spontaneous flow. The actual rate of lymph flow in these normal limbs is, therefore, somewhat artificial and probably not very accurate, but the general trend, increase or decrease, can be determined. When the paws of a normal dog are cooled by immersion in ice-water or warmed by immersion in water at 37, 45 or 50° C., there are no very considerable changes in lymph flow. Table 2 shows the effect of cooling in a typical experiment. In this dog the

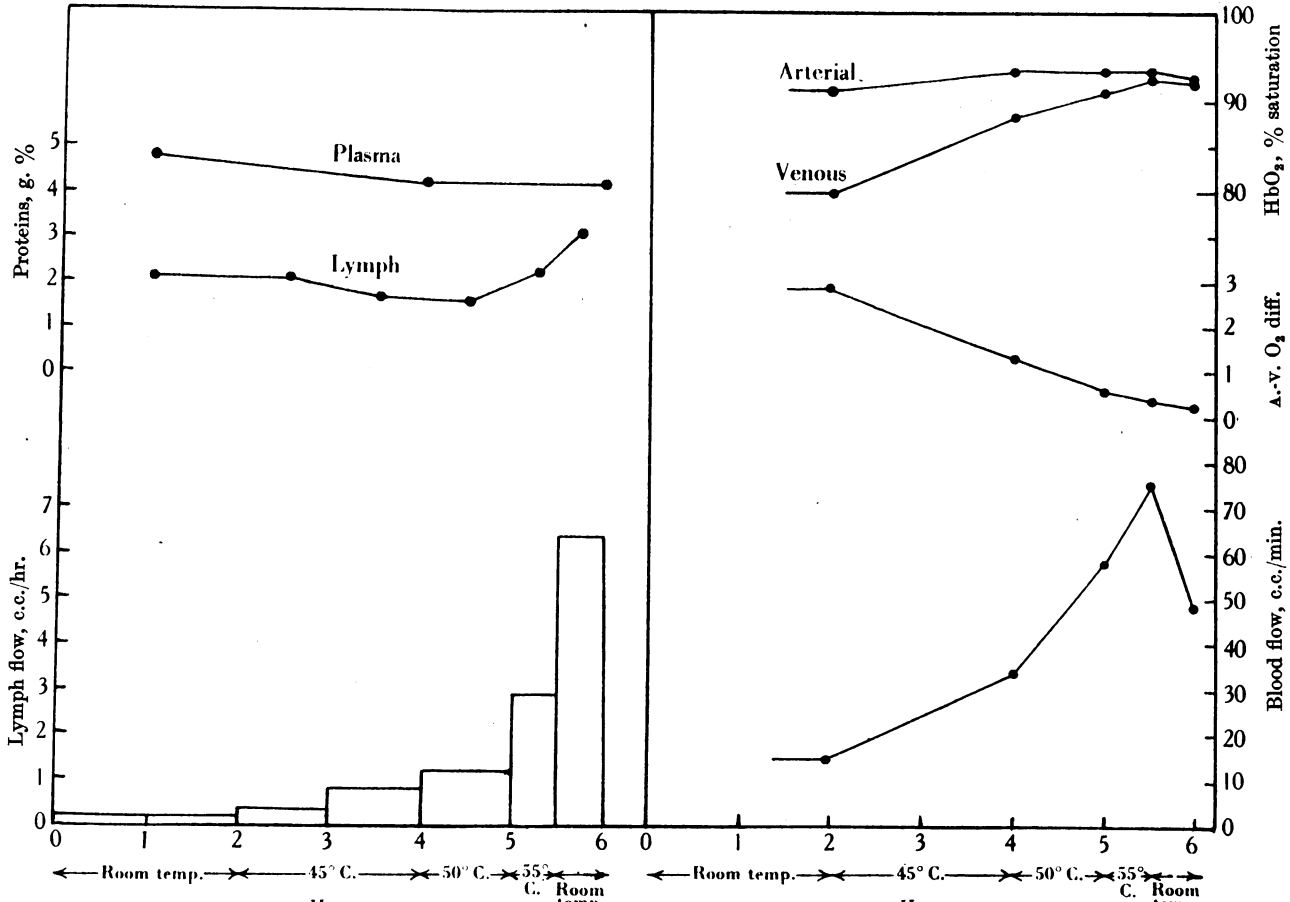
TABLE 2. The effect of cold on the lymph flow from the forepaw of a normal dog under nembutal anaesthesia

	Time hr.	Lymph flow c.c./hr.	Lymph proteins g. %
Room temp.	0–1	0·9	1·5
	1–2	1·1	1·4
Ice-water	2–3	0·7	1·4
	3–4	0·3	1·4

hindleg lymph duct was cannulated. The effect of cooling the paw was to slow down the lymph flow, without altering the protein composition of the lymph.

In Text-fig. 6 the effects of warming the forepaw on the lymph flow from the duct just above the ankle joint are shown. The lymph flow increases somewhat when the paw is immersed in water at 45° C., and still further on immersion in water at 50° C. This increased flow is accompanied by a slight fall in the protein concentration of the lymph. When the foot is then immersed in water at 55° C., the lymph flow increases abruptly, the protein concentration of the lymph rises and the paw becomes oedematous. Lassar (1889) demonstrated that when a dog's paw is immersed in water at 54° C. it becomes oedematous and the lymph flow increases.

These experiments show that temperatures as low as 0° C. and as high as 50° C. do not affect the permeability of the capillaries of the dog's paw to proteins, but at 55° C. the capillaries are damaged and the osmotic balance between the plasma and tissue fluid is upset by the increased leakage of



Text-fig. 6. The effects of warming the paw of a dog, on lymph flow, lymph and plasma proteins, blood flow, A.-V. O_2 difference and Hb saturation. Mean of two experiments.

proteins through the capillary membrane. The decrease in lymph flow on cooling may be explained by a decreased filtration of fluid through the capillaries caused by a decreased blood flow, and the increased lymph flow on warming up to 50° C. is the result of an increased formation of normal capillary filtrate following an increased blood flow. The capillary filtrate has a lower concentration of protein than tissue fluid, and so the protein concentration of tissue fluid and lymph falls somewhat as the paw is warmed, until a temperature is reached, 50–55° C. in the case of the dog's paw, where the capillary membrane is damaged. Then the capillary filtrate contains a high concentration of protein with a resultant increase in the protein concentration of tissue fluid and lymph, and a local upset in the osmotic balance.

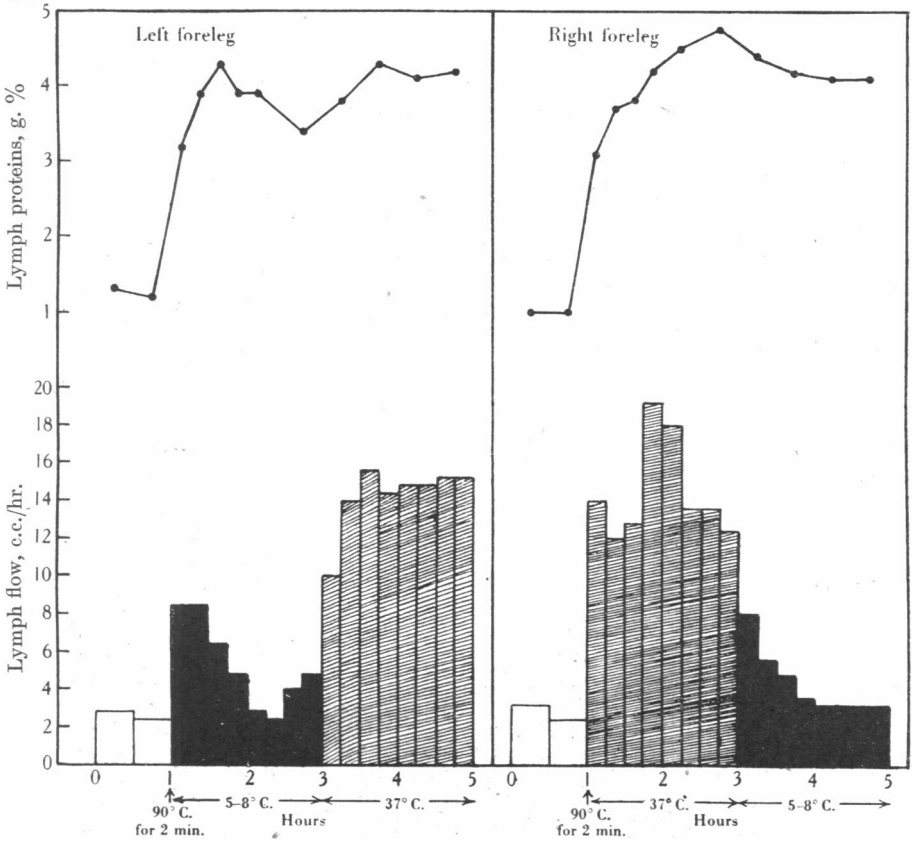
Lymph flow in scalded paws. Experiments in which the forepaws of dogs have been scalded by immersion in water at 80° C. for 2 min. or 90° C. for 2 min. and then allowed to remain at room temperature show that, after the burn, the lymph flow is greatly increased and the protein concentration of the lymph is raised to approximately the level of the plasma proteins. These results agree with the data of Field, Drinker & White (1932), Glenn, Peterson & Drinker (1942) and Glenn, Muus & Drinker (1943), and will not be given in detail.

In another series of experiments, the lymph ducts of both forelegs were cannulated, lymph collected and then both forepaws were immersed in water at 90° C. for 2 min. or 80° C. for 1½ min. One forepaw was then placed in ice-water or water at 5–8° C. and the other in water at 37° C. Lymph was collected for 2 hr., after which time the water-baths were reversed. Text-fig. 7 depicts the results of a typical experiment.

In these experiments the lymph flow before scalding was obtained by massage, but after scalding was spontaneous. In Text-fig. 7 the left forepaw was placed in water kept at 5–8° C., while the right forepaw was placed in a water-bath at 37° C. immediately after scalding. The lymph flow from both forepaws increased and was spontaneous, but the flow from the right side was very much greater than that from the left side. At the end of 2 hr. the right paw was swollen much more than the left. On reversing the water-baths, the flow from the left paw, now in water at 37° C., increased considerably, while the flow from the right paw, now in water at 5–8° C. decreased. Other experiments in which the paw was left at 0, 37 and then 45° C. after scalding show clearly that the lymph flow increases as the local temperature increases.

In these experiments the local cooling of the scalded paw decreased the swelling of that paw compared with the one kept warm, and, as a result, decreased the lymph flow. Even after the paw had been kept warm for 2 hr. after scalding, local cooling had a rapid effect in decreasing the lymph flow, which is an indication that the formation of oedema fluid was being decreased.

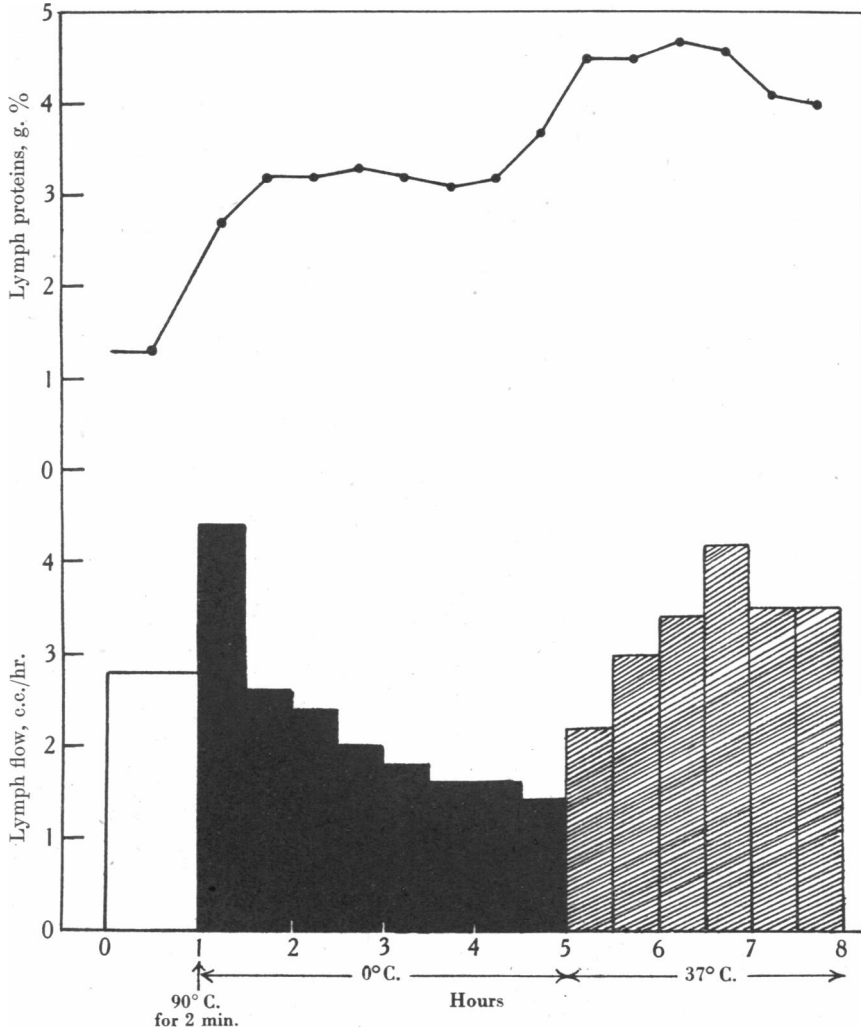
The protein concentration of the lymph in all cases rose considerably after scalding. There is an indication in all experiments that the protein level is slightly higher when the paw is kept warm than when it is kept cold. In Text-fig. 7 it can be seen that in the left paw there is a tendency for a fall after the initial sharp rise with the paw in water at 5–8° C., a fall which is reversed



Text-fig. 7. The effect of local temperature on the lymph flow from the forepaws of a dog scalded in water at 90° C. for 2 min.

when the paw is put in water at 37° C. In the right paw the protein concentration goes on rising when at 37° C., and then falls when the paw is put in ice-water. A similar effect was seen in other experiments. In Text-fig. 8 the protein concentration of the lymph after scalding, with the paw in ice-water, is fairly constant at a level of about 3·2%. When the paw is then kept at 37° C., the lymph flow increases and the protein concentration in the lymph rises to between 4·0 and 4·6%, which was the level of the plasma proteins.

It appears, therefore, that by cooling the scalded paw, not only is the production of tissue fluid slowed down, but the protein concentration of that fluid is also somewhat less.

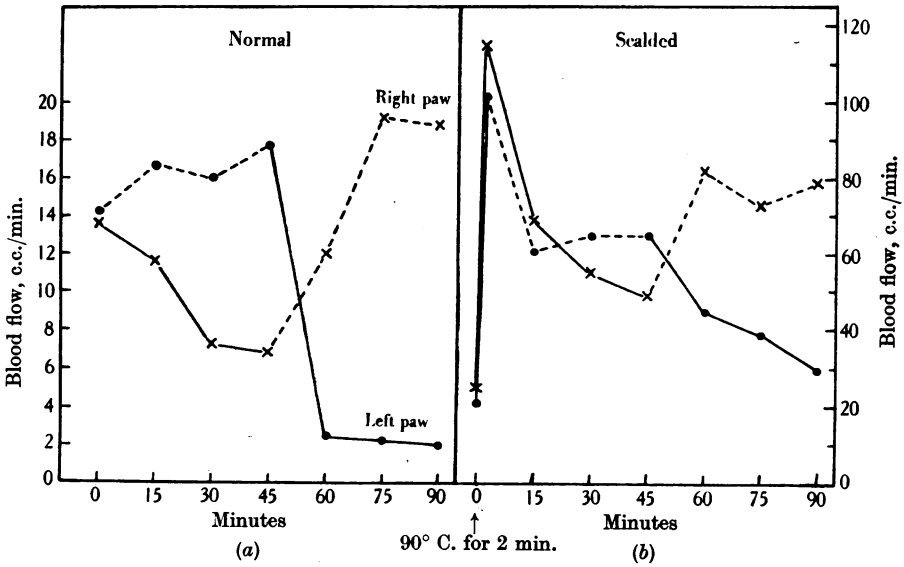


Text-fig. 8. The effect of local temperature on the lymph flow from the forepaw of a dog scalded in water at 90° C. for 2 min.

The effects of local temperature on the blood flow

The experiments so far described show that the tissue fluid formation after scalding increases with an increase in local temperature. This suggests that the blood flow through the damaged part is the determining factor. The blood flow has been determined in anaesthetized, heparinized dogs.

The effects of cooling or warming the normal paws of a dog are shown in Text-fig. 9. Immersion of the left paw in a water-bath at 37° C. and of the right paw in ice-water increased the flow in the former and decreased the flow in the latter. On reversing the water-baths, the flow in the left paw, now in ice-water, fell considerably, while the flow in the right paw, now at 37° C., rose. Text-fig. 6 also shows the effect of warming on the blood flow and the arteriovenous oxygen difference. As the blood flow increases, the arteriovenous oxygen difference decreases.



Text-fig. 9. (*a*) The effect of local temperature on the blood flow through the forepaws of a normal dog. Mean of two experiments. (*b*) The effect of local temperature on the blood flow through the forepaws of a dog after scalding in water at 90° C. for 2 min. Mean of two experiments ——— Local temp. 0° C. ---- Local temp. 37° C.

When the paws of a dog are scalded, the blood flow immediately increases greatly as shown in Text-fig. 9*b*. If one paw is then kept at 37° C. and the other at 0° C., the blood flow falls in both, but to a much lower level in the paw kept cool. When the warm paw is now placed in ice-water, there is a rapid fall in the blood flow, and when the cold paw is placed in water at 37° C. there is a sharp rise in blood flow.

Except for the experiments represented in Text-fig. 6, the determinations of blood flow have been made for only 1½ hr. after the initial readings were obtained, with the paws kept for ¾ hr. at 37° C. and ¾ hr. at 0° C. Although the dogs were heparinized, there was always the risk of clumps of platelets forming at the ends of the cannulae, so this risk was minimized by keeping the time of the experiment relatively short. By comparison with the effects

on lymph flow, it seems that the blood flow would be still more decreased had the paw been kept longer in ice-water.

Hastings (1820), while studying problems of inflammation, showed that if the web of a frog's foot is scalded, the blood flow is accelerated and that the application of ice caused contraction of the vessels and a reduced circulation rate. (I am indebted to Prof. G. R. Cameron for this reference.)

It is, therefore, evident that cooling the limb after a burn greatly reduces the blood flow through the damaged area, as it does in a normal limb. The effect of local temperature on the oedema formation after scalding depends, therefore, on the effect on the blood flow through the injured part.

The effects of decreasing blood flow in the scalded hindlegs of rabbits by tying the femoral artery

The blood flow to the hindleg of rabbits was decreased by ligaturing the femoral artery immediately after scalding. By thus cutting down the blood supply to the injured area, the rate of oedema formation was greatly reduced. In one experiment, both hindlegs of four rabbits each weighing 2·0 kg. were scalded as previously. Immediately after scalding, the femoral artery on one side was ligatured and cut. Both hindlegs were then kept in a water-bath at 37° C. for 6 hr. The leg with the femoral artery tied showed practically no swelling while the other was greatly swollen, the mean difference in weight being 39 g.

In a second experiment, one leg was scalded and the artery tied immediately after. Both legs were then kept in a water-bath at 37° C. Four groups of rabbits, each group consisting of two animals of average weight 2·3 kg., were kept thus for 2, 6, 12 and 24 hr. respectively. The average increase in weight of the scalded leg was 8, 8, 25 and 31 g. respectively, which is very much less than the increase with the femoral artery intact (cf. Text-fig. 1).

In a third experiment, both hindlegs of three rabbits were scalded and both femoral arteries were tied immediately after scalding and the legs kept at 37° C. for 24 hr. Blood samples were taken for the estimation of haemoglobin and plasma-protein concentration; mouth temperature was also determined. The mean results are given in Table 3. These figures show very little haemo-concentration and change in plasma proteins and mouth temperature as compared with animals without ligature of the femoral artery (cf. Text-fig. 3).

In a control group of ten rabbits in which the femoral artery was ligatured and cut on one side, no ill-effects were observed in that leg, the rabbits behaving normally. Thus the collateral circulation is sufficient for the normal needs of the tissues in rabbits kept in cages at comparative rest.

The results of these experiments show that the oedema formation after burning varies with the blood flow, and support the suggestion that cold acts in decreasing the oedema by lessening the blood flow through the injured limb.

TABLE 3. The Hb percentage, plasma-protein percentage, and mouth temperature in rabbits after scalding both hindlegs and then immediately tying both femoral arteries. Mean of three animals

	Hb %	Plasma protein g. %	Mouth temp. ° F.
Before nembutal	82	5·6	101·7
After nembutal	80	4·8	—
Scalding:			
1 hr. after	83	—	98·6
2 „	81	5·0	99·0
4 „	82	4·8	100·6
6 „	82	4·6	101·8
12 „	83	4·5	101·6
24 „	82	4·7	102·4

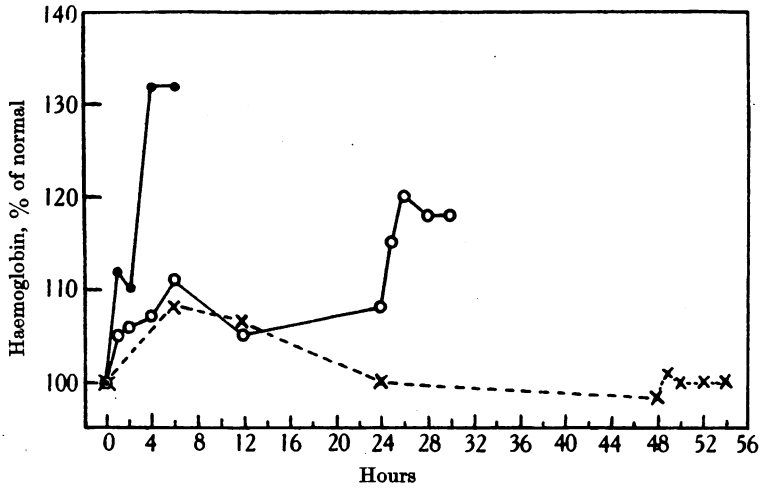
Effect of local temperature on recovery of the capillaries after a thermal burn

So far it has been shown that cold decreases the formation of oedema after thermal injury. Cold also lessens the metabolism of cells, and might, therefore, have a retarding effect on the recovery of the damaged tissue. Normally, the excess oedema formation through the injured capillaries ceases about 48 hr. after burning. Experiments were designed, therefore, to see whether, when the cold treatment ceased and the limb was then kept warm, the oedema fluid formation would suddenly increase and thereby cause latent haemoconcentration.

Both hindlegs were scalded in the usual way in three groups of rabbits. The legs were then kept in ice-water for 2 hr. in one group, 24 hr. in the second group, and 48 hr. in the third group. After being kept cold for these times the legs were immersed in a water-bath at 37° C. for 4–6 hr. Blood samples were taken and haemoglobin estimated. The haemoglobin is given as a percentage of the pre-burning level, and the results are depicted in Text-fig. 10. In the first group the haemoglobin rose to about 110% in the first 2 hr. in ice-water and then increased suddenly to 132% when kept warm. In the second group there was slight haemoconcentration during the first 24 hr., and when the legs were then kept warm, the outpouring of fluid caused a sudden increase in haemoglobin to about 120%. In the third group there was slight haemoconcentration during the first 24 hr. with a return of the haemoglobin to normal by 48 hr. The effect of warming the legs in this group was to cause only a very small increase in the haemoglobin.

Thus, the longer the injured part is kept cool up to 48 hr., the less will be the haemoconcentration when this part is warmed. The fact that after 48 hr. there is but little increase in haemoglobin when the legs are warmed does not necessarily mean that the capillary damage has been completely repaired by then, but it appears that after this time there will be no sudden increase in oedema fluid formation on warming, likely to cause any appreciable circulatory disturbance.

In another group of experiments to find whether cold for 48 hr. retards subsequent healing, small burns were made on the outer side of each hindleg in three rabbits. The burns were made by a closed, hollow copper cylinder, 2 in. long and $\frac{1}{2}$ in. in diameter. Water at 75° C. flowed continuously from a reservoir through an inlet near the bottom and out through an outlet near the top. This cylinder was held on the shaved skin of the rabbit's leg for 45 sec., producing a circular burn, $\frac{1}{2}$ in. in diameter. Two such burns were made on each leg. One leg of each rabbit was then kept in ice-water for 48 hr. and the other leg in a water-bath at 37° C. for 48 hr. After that time, the rabbits were



Text-fig. 10. The haemoglobin in three groups of rabbits after scalding both hindlegs. •——• Local temp. 0° C. for 2 hr. and then 37° C. for 4 hr. o——o Local temp. 0° C. for 24 hr. and then 37° C. for 6 hr. ×----× Local temp. 0° C. for 48 hr. and then 37° C. for 6 hr.

allowed to remain in their cages at room temperature. The burns were found to heal at about the same rate on each leg, the mean healing time of the six burns kept cold being 17·1 days and that for the six kept warm 17·5 days.

In a further group of six rabbits, one burn was made on each leg. The femoral artery on one side was then immediately ligatured and cut. The burns healed at exactly the same time on both sides, the mean time being 15·3 days.

It is evident, therefore, that by decreasing the blood flow to a limb by the application of cold or by ligaturing the main arterial supply, the healing time of a small burn is not affected. The cold applied to local burned areas should thus not have a deleterious effect on the subsequent course of the burn, but only a beneficial effect in lessening and slowing the degree of local fluid loss.

Comparison of the effects of cold and of pressure bandages

To compare the effects of close-fitting plaster bandages with those of cold on the local fluid loss, one hindleg of each rabbit of four groups (four in each group) was scalded as above. Immediately afterwards, a plaster of Paris bandage was applied up to a level above that of the burn. Both normal and burned legs were then kept in a water-bath at 37° C. for 2, 6, 12 or 24 hr., when the animal was killed and the hindlegs dissected and weighed. The average amount of fluid loss in each of these four groups (each group averaged 2·3 kg. body weight) was 17, 21, 23 and 22 g. respectively. These figures are of the same order, but slightly less than those obtained for cold (cf. Text-fig. 1). The amount of oedema depends largely on how tightly the bandage is applied. In these experiments the bandages were very closely applied.

Discussion

The local loss of fluid

Provided a burn is not severe enough to cause almost complete coagulation and necrosis of the injured part, the local loss of fluid plays a considerable part in the subsequent course of the burn, especially in the early stages. The burns employed in this investigation have been of sufficient severity to damage the local capillaries, but not to produce coagulation of the limb. A rabbit's ear, for example, will shrivel up if placed in water at 90° C. for 2 min., whereas a dog's paw will not. Prinzmetal, Bergman & Hechter (1944) have also shown in rats that a leg immersed in water at 75° C. for 10 sec. will become very oedematous, whereas a leg immersed in water at 100° C. for 2–3 min. shows little oedema. Thus burns of different severity have been used here for different animals, since only one factor, fluid loss, has been studied.

In the present series of experiments with rabbits, it has been shown that when only one hindleg is scalded to a level just below the knee joint and then kept warm (37° C.), the local fluid loss is 2·5% of the body weight after 2 hr., 2·9% after 6 hr., 3·6% after 12 hr., and 3·8% after 24 hr. Since the fluid lost from the circulation closely resembles plasma in composition, these figures represent a very considerable and sudden plasma loss, being more than half the original plasma volume (Courtice, 1943). Even though modern treatment by plasma transfusions can replace plasma loss, it is obviously important to decrease and slow down the amount of oedema formation as much as possible.

It is the effect of this fluid loss on the plasma volume which is of primary importance. Hence the rate of fluid loss is as much a determining factor as the actual amount. The fall in plasma volume is determined by the balance between the local plasma loss and the tissue fluid withdrawal from the undamaged tissues into the blood stream. In haemoconcentration due to thermal

burns and other agents (Courtice, 1943; Cameron *et al.* 1945; Cameron & Courtice, unpublished results), the haemoglobin percentage reflects fairly accurately the changes in plasma volume. Thus in the experiments described above, during the first 6 hr. after the burn in rabbits with both hindlegs scalded below the knee and then kept at 37° C., the fluid loss is greater than the withdrawal of tissue fluid into the circulation, although this latter must be considerable, for the loss of plasma in 2 hr. is about equal to the original plasma volume, and yet the haemoglobin is increased to only 130% of the normal value. From about 6 hr. onwards, the outpouring of plasma continues, but at a slower rate (Text-fig. 1), and the withdrawal of tissue fluid into the circulation together with fluids by mouth must exceed the fluid loss, for the haemoconcentration decreases. The fall in the plasma-protein concentration is also an indication of the fluid loss and of the degree of withdrawal of tissue fluid into the blood stream. This fall in the plasma protein and the rise in the haemoglobin percentage run parallel with the amount and rate of fluid loss, which in turn vary with the local temperature.

A slowing effect of cold on oedema formation after traumatic injury has been described by Blalock (1942). He investigated the effects of local application of heat and cold to the traumatized limbs of anaesthetized dogs. The survival time of dogs whose injured limbs were kept cold was twice as long as those whose limbs were kept warm. These experiments suggested that the cold lessened the rate of oedema formation, but that the trauma was severe enough to produce death in spite of this slowing.

Rose (1936) has used cold-water treatment in human burns, by immersing the whole body in a bath as well as swabbing the local burned areas with cold water. He maintains that especially in the initial phase much benefit is derived from this treatment, relief from pain being marked.

The lymph and blood flow

Evidence of the mechanism in the slowing of oedema formation when the injured limb is cooled is given in the experiments on lymph and blood flow in the dog. In a normal dog's paw, the lymph and blood flow are slowed by cooling in ice-water and increased by immersion in water up to 50° C. without any apparent injury to the capillaries. The lymph-flow changes are not very great until a temperature of about 55° C. is reached, when the capillary permeability is increased and the protein concentration of the lymph increases.

After a thermal burn in which the capillaries become freely permeable to the plasma proteins, the lymph flow varies with the rate of tissue fluid formation. As the protein concentration in the tissue fluid becomes approximately the same as that in the plasma, the osmotic balance at the capillary membrane is upset, so that there is probably little if any reabsorption of capillary filtrate into the blood stream. The lymphatics, therefore, carry away the excess tissue

fluid, and the faster the tissue fluid is formed the greater is the lymph flow. The effect of local temperature on the tissue fluid formation can, therefore, be gauged by the lymph flow, at least in the early stages before much clotting of the fluid occurs. Cooling of the dog's scalded paw results in a lessening of the lymph flow as compared with warming the paw, which indicates a lessening of the filtration through the capillaries with a resultant decrease in tissue fluid formation.

The primary cause of the effect of local temperature on the fluid loss seems to be the blood flow. In a normal limb, the blood flow decreases on cooling and increases on warming, but these changes in blood flow do not cause very appreciable alterations in tissue fluid nor in lymph flow. The fluid balance seems, therefore, to be controlled mainly at the blood capillary. When a limb is scalded, however, the osmotic balance is upset with little or no capillary reabsorption. The effect of alterations of blood flow on tissue fluid formation are then considerable, as has been seen above. The only removal of the fluid is by the lymphatics, which cannot deal efficiently with such a rapid outpouring of fluid. Thus, by keeping a good blood flow through the injured part by warmth, the tissue fluid formation is considerable, whereas by decreasing the blood flow and probably also the capillary pressure, by cooling, the amount of oedema formation is lessened.

It has also been noted that the lymph-protein concentration is somewhat less when the scalded limb is kept cold than when it is warm. It may be that the cold causes contraction of the capillaries which renders them less permeable to the proteins, whereas warmth causes dilatation which stretches the walls of the capillaries and makes them more permeable. Another factor which may be involved is the capillary pressure, which is probably lower in the cold limb with a decreased blood flow and presumably contracted arterioles.

It is evident from the results described that the local application of cold considerably lessens the oedema formation after scalds in rabbits, goats and dogs. From the results of small burns in rabbits and of the effects of sudden warming after keeping the injured legs cold, it appears that the application of cold for 48 hr. does not have any appreciable slowing effect on the ultimate recovery of the burn. Thus, so long as the general body temperature is maintained, the local application of cold should lessen the fluid loss and so lessen the tendency to circulatory collapse, especially if applied in the early stages. From the work of other investigators, it appears that cold might decrease pain (Rose, 1936; Smith, 1942) and bacterial infection (Crossman, Ruggiero, Hurley & Allen, 1942; Mock & Mock, 1943), two other important features in burns.

Summary

1. The effects of local temperature on the fluid loss after thermal burns in rabbits, goats and dogs have been investigated.

2. The legs of these animals have been scalded by immersion in hot water—rabbits at 75° C. for 45 sec., goats at 85° C. for 2½ min., and dogs at 80° C. for 1½ min. and 90° C. for 2 min. After scalding, the injured parts have been kept at a constant temperature by immersion in water at 0, 37 or 45° C.

3. The amount of local fluid loss when one leg of a rabbit is scalded is nearly three times as great when the leg is afterwards kept at 37° C. as when it is kept at 0° C. Not only is the rate of oedema formation decreased, but, up to 24 hr., the actual amount of oedema is also decreased.

4. In rabbits and goats with both hindlegs scalded, one leg kept in ice-water always showed much less oedema than the other kept in water at 37° C.

5. The effect of the local temperature after scalding on haemoglobin content, plasma-protein concentration, blood pressure, plasma non-protein nitrogen and mouth temperature has been determined in rabbits. The degree of haemoconcentration runs parallel with the degree of plasma loss, which in turn varies with the local temperature. A burn which might cause death from circulatory collapse if the injured part were kept very warm might not if the part were kept cold.

6. The application of cold after the scalded legs have been kept warm for 2 hr. rapidly causes a decrease in the rate and amount of fluid loss and also in haemoconcentration.

7. Plasma and serum transfusions are more effective in reducing haemoconcentration when the injured part is kept at 0° C. compared with 37° C.

8. The lymph flow from the scalded paws of anaesthetized dogs is much less when the injured part is kept cold than when it is kept warm. The protein concentration of the lymph is also slightly less when the paw is cold than when it is warm.

9. The blood flow through the scalded paw of a dog is greatly decreased by the application of cold as compared with warmth.

10. The plasma loss in a scalded limb appears to depend upon the blood flow which can be altered by altering the local temperature. In experiments in which the blood flow in the scalded legs of rabbits was decreased by tying the femoral artery, the plasma loss and haemoconcentration were also greatly reduced.

11. A decreased blood flow, caused by ice-water for 48 hr. or by ligature of the femoral artery, had no effect on the subsequent recovery of small burns in rabbits.

12. The effects of cold are comparable to those of pressure bandages when applied to the scalded legs of rabbits.

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