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The Influence of Body Temperature on Traumatic Vasospasm

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ABSTRACT

The effect of hypothermia on traumatically induced vasospasm was studied in an in vivo model of the rabbit ear artery. Spasm was induced by standardized compression of a 3.2 mm segment of the artery for 3 s. The internal diameter was continuously measured with the aid of an operating microscope during transillumination of the artery. Measurements were begun before spasm induction and continued until the spasm was completely resolved. Spasm was first induced at normothermia and then after reduction of the body temperature by 1.0°C and 1.75°C. The spasm was evaluated in terms of its duration, intensity (% reduction of initial diameter) and severity (area under the curve where diameter was plotted against time). The results were compared with those in a control group which was kept normothermic. Reduction of the body temperature caused a significant increase in the duration of the spasm and increased its severity, but did not influence its intensity.

INTRODUCTION

Microvascular techniques are well established in several surgical disciplines. These procedures can be attended with very specific complications. One of them is a local increase in vascular tone, which frequently occurs at the site of a microvascular anastomosis. This vasospasm is sometimes so severe that it can jeopardize the patency of such an anastomosis and the success of the procedure.

The pathophysiology of vasospasm occurring after microvascular procedures is not known. One factor which has been suggested as a cause of aggravation of the spasm is local cooling, this effect of local cooling has been used in an experimental model for investigation of vasospasm occurring in connection with microvascular surgery (10). The importance of maintaining a normal body

temperature during microvascular surgery in patients in order to prevent vasospasm has been pointed out by several authors (13,16,7,1,2). This opinion is not, however, based on experimental or clinical studies and to our knowledge the effect of general hypothermia on traumatic vasospasm has not yet been investigated. We have therefore tested the hypothesis that a decrease in body temperature aggravates traumatically induced vasospasm.

MATERIALS and METHODS

Animals

Ten adult long-eared loop rabbits of both sexes, with a body weight of 2.4-4.4 kg, were used. They were housed under standardized environmental conditions with free access to water and food for two weeks prior to the experiments, in accordance with the institution's guide for the care and use of laboratory animals.

Animal preparation

The animals were anesthetized with alphaxolone-alphadolone (Althesin^{R}, Glaxo), 3 mg/kg given intravenously and diazepam (Diazemuls, Kabi Vitrum,), 2 mg/kg intramuscularly (i.m.). During this short-lasting anesthesia the sensory nerve running parallel to the central ear artery was cut at the base of the left ear. This made it possible to perform the rest of the experiments with only light sedation, produced by 0-2 further injections of 1 mg/kg diazepam given intravenously. The rabbits were kept in a specially designed open box. A warming water blanket (Aquamatic K-20-D, Hamilton, Cincinatti, Ohio, USA) was laid over their backs and was set at 37°C. The central body temperature was measured continuously with a rectal thermometer. The experimental set-up is shown in Fig. 1.

The skin was incised along the left ear artery and the wound edges were everted with a continuous suture (Fig. 1; right inset). The wound was moistened with Ringer-acetate and covered with plastic polyethylene foil (Glad Pack^{R}, Union Carbide) in order to maintain a constant environment in the wound.

The preparation of the vessel caused an initial, transient vasospasm, which spontaneously resolved in approximately 10 min. To allow the vessel to regain complete normality a minimum of 30 min was always allowed to elapse between the initial preparation and the conduction of the first experiment.

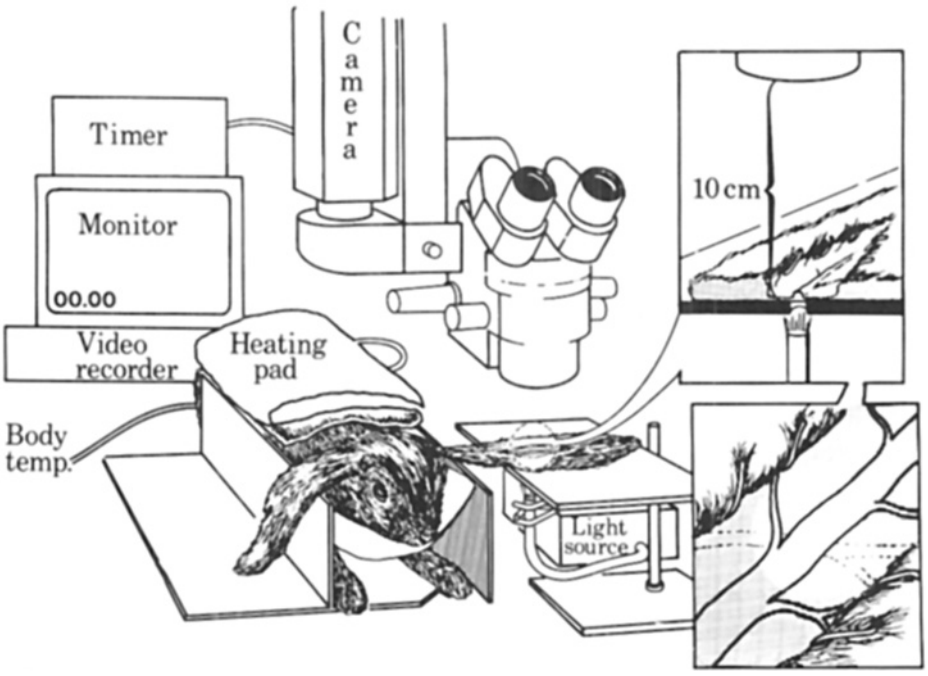

Fig. 1. An artist's view of the experimental set-up.

Induction of vasospasm

Vasospasm was induced with a Wachenfeldt clip-applying forceps (Fig. 2; Stille-Werner, Stockholm, Sweden), with an occlusion area of 3.2 x 1.4 mm = 4.5 mm^2. At rest it is closed and exerts a standardized compression force of 2.45 N at an area of 4.5 mm^2, i.e. a pressure of 5.45 x 10^5 N/m^2, between its claws. The ear artery was pinched with the forceps for 3 s. A first pinch was made on the distal part of the ear, and two further pinches were made proximal to the first one.

Measurement of the inner diameter

The ear was fixed with needles to a specially designed cork board which allowed the central ear artery to be transilluminated with cold light (Intralux-500, Volpi AG, Switzerland). The artery was then inspected from above with an operating microscope equipped with a 25 X objective with a focal distance of 100 mm and a JVC video color camera. The inner diameter of the artery was measured directly on the video monitor. The resolution of the set-up was determined after calibration with a Leitz micrometer ruler and found to be 0.01 mm. The first measurement was made in the undisturbed vessel, whereafter spasm was induced and measurements were repeated every min

until no visible spasm remained, i.e. when there was no narrowing of the traumatized segment compared with the neighboring nontraumatized vessel segment.

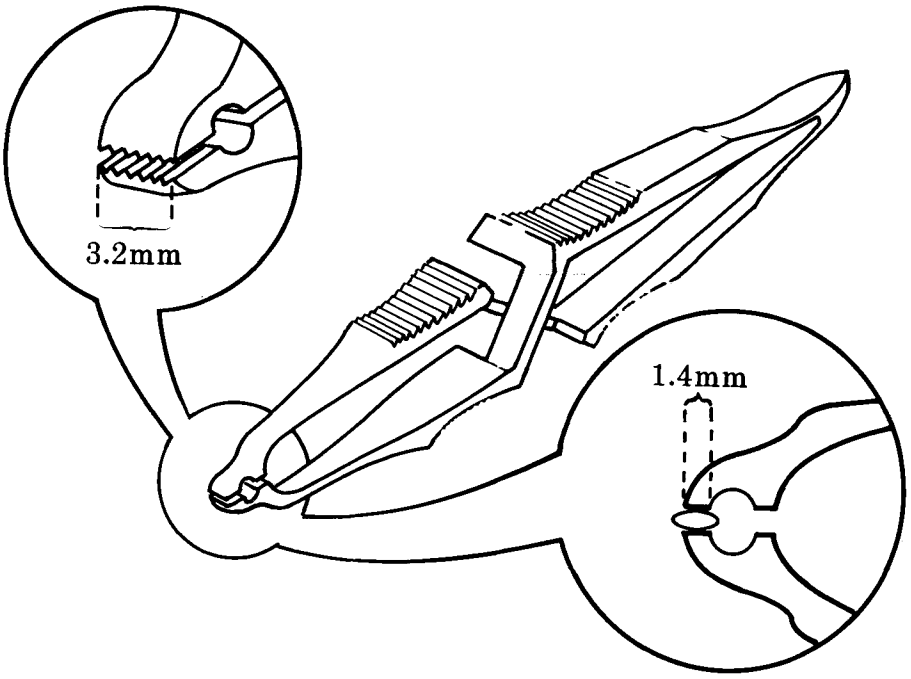

Fig. 2. A schematic view of the Wachenfeldt clip-applying forceps.

Experiments

A. Experimental Group: n=5.

One episode of spasm was first induced at normal body temperature. The core temperature was then lowered by applying a plastic bag filled with ice cubes to the back of the animal. This lowered the body temperature at a rate of 1.8°C per hour, at which rate the diameter of the artery remained unchanged. When the core temperature had fallen by close to 1.0 and by 1.75°C episodes of spasm were again induced. Blood samples for determination of serum cortisol were taken before reduction of the body temperature and just before the first induction of spasm after the cooling. They were immediately centrifuged, frozen to -70°C and later analyzed with an RIA method.

B. Control Group: n=5.

These experiments were performed as in the experimental group, but the animals were kept normothermic throughout the study period.

Variables

The following variables were measured or calculated and are depicted in Fig. 3.

D_I: the initial inner diameter of the vessel.

D_M: the inner diameter during maximal spasm.

D_F: the final inner diameter when the spasm was resolved and when the inner diameter of the traumatized vessel segment was the same as that of the adjacent vessel segment.

T_0: the time of removal of the forceps from the traumatized vessel.

T_M: the earliest time of maximal spasm; D_M.

T_F: the duration of spasm; the time of D_F.

The following four variables were thereafter used in the descriptive and statistical analysis of the vasospasm.

1. **The initial diameter,** D_I, before and after reduction of the body temperature.
2. **The duration of the spasm,** T_F
3. **The intensity of the spasm,** given in percent and defined as $(D_I - D_M)/D_I \times 100$
4. **The severity of the spasm,** calculated as the area D x T, defined as the integrated decrease in diameter from T_0 to T_F (shaded area in Fig. 3).

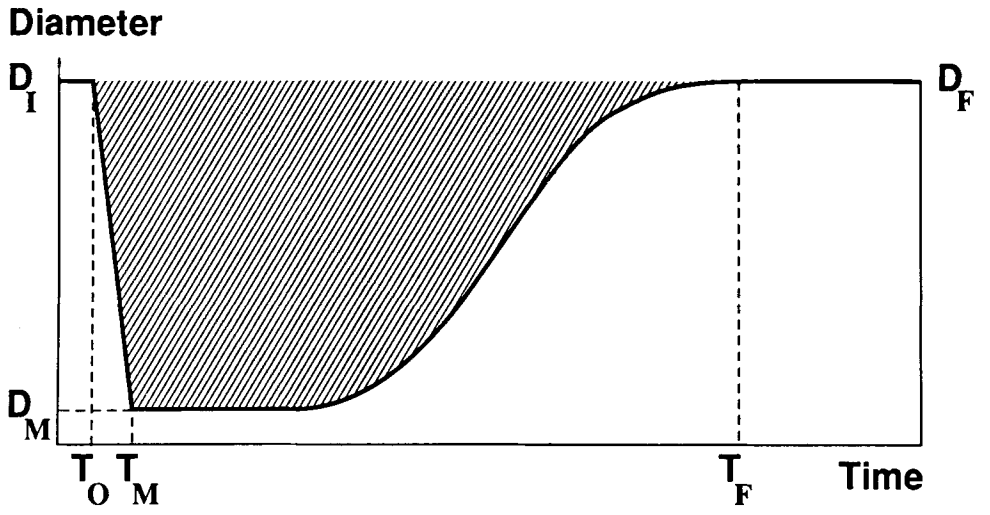

Fig. 3. A graph in which the diameter is plotted over time. The different variables are defined in the Materials and Methods section.

Statistical evaluation

The difference between the first, controle spasm and each of the two experimental spasms was calculated for each animal, both in the experimental and the control group. The two groups were then compared regarding these differences by Student's two-sample t test. All data are given as mean ± SEM. A difference at the 5% level is regarded as significant and is indicated by an asterisk in the figures.

RESULTS

During the experiments the rabbits were very calm and relaxed in their boxes and the experimental set-up did not appear to disturb the awake rabbit to any appreciable extent. The body temperatures of all animals at the different measurment times are shown in Fig. 4.

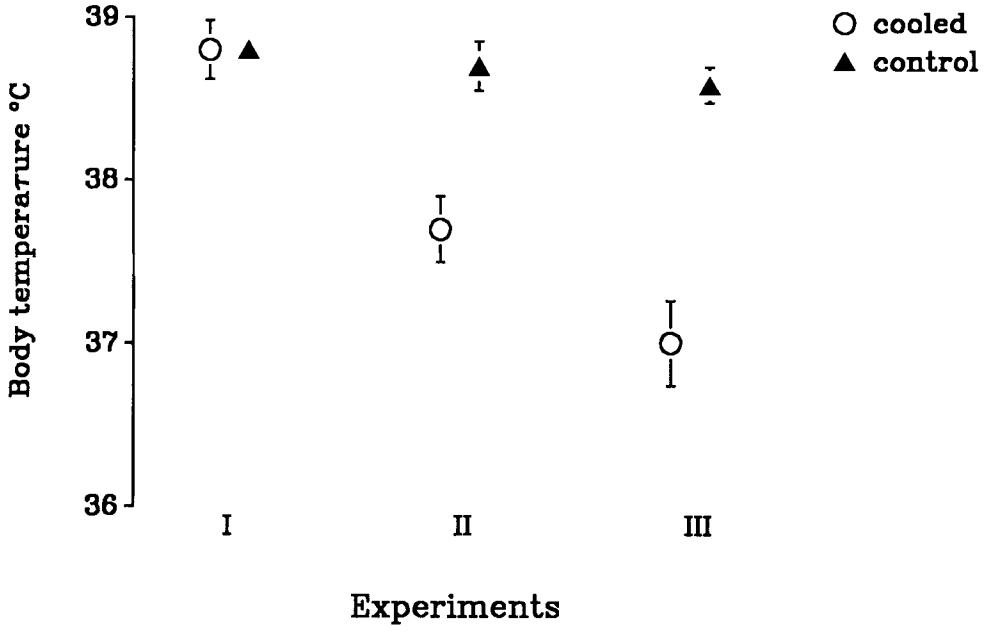

Fig. 4. Body temperature, in degrees Celcius at the time of the experiments in the experimental and control groups. The temperature decreased by close to 1.0(degrees Celcius) in the experiment 2 and 1.75(degrees Celcius) in experiment 3. N=5 in all experiments.

At the first level there was a decrease in body temperature varying from 0.8 to 1.1°C and at the second level the body temperature had decreased by 1.1-2.0°C. The exposed left central ear artery could be readily observed with the cold light transillumination. In the undisturbed vessel the outer and inner diameters were very similar (Fig. 5 A), but after induction of vasospasm these diameters were easily separable (Fig. 5 B). After a 3-s pinch with the forceps, the central artery reacted with vasospasm. The constricted segment was limited to the pinched area. The spasm was maximal within 1 min and the inner diameter was decreased to approximately 15% of the original value. This intense constriction remained virtually stable for 5 min, whereafter it slowly resolved.

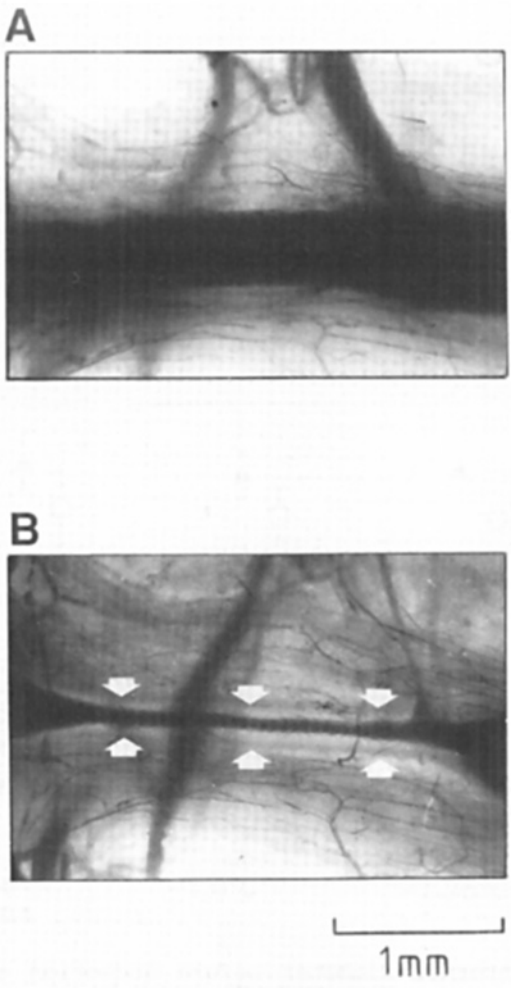

Fig. 5. The appearance of an undisturbed (A) and a spastic (B) vessel segment. The arrows indicate the border of the tunica muscularis.

The internal diameters before induction of vasospasm were similar in the two groups and at all times (Fig. 6). Hypothermia caused a significant increase in the duration of spasm, whereas the duration was similar in the three different experiments in the control group (Fig 7). Furthermore, the severity of the spasm was also significantly increased in the hypothermic animals compared with the controls (Fig 8). The intensity of the spasm, i.e. the relative decrease in diameter, remained unchanged during hypothermia (83.8 ±5.3% at -1.75°C) compared with the value in the control group (85.8 ±3.3%). The serum cortisol levels were not affected by the ice cooling of the animals(282 ±27 mmol/l and 286 ± 29 mmol/l after).

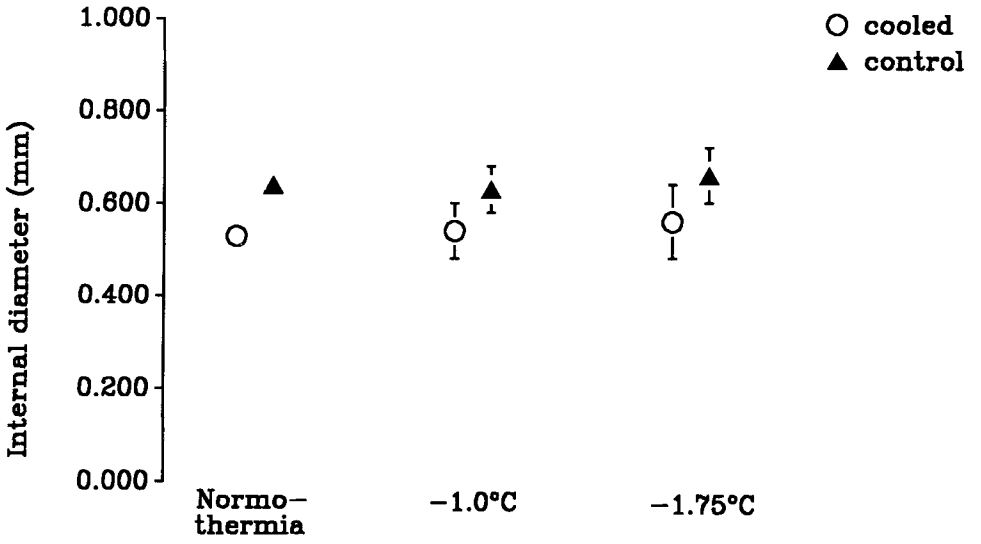

Fig. 6. The internal diameter before induction of spasm. The body temperature in the cooled group was reduced by close to 1.0 and 1,75°C in experiment 2 and 3, respectively. The control group was kept normothermic in all three experiments. N=5 in all experiments

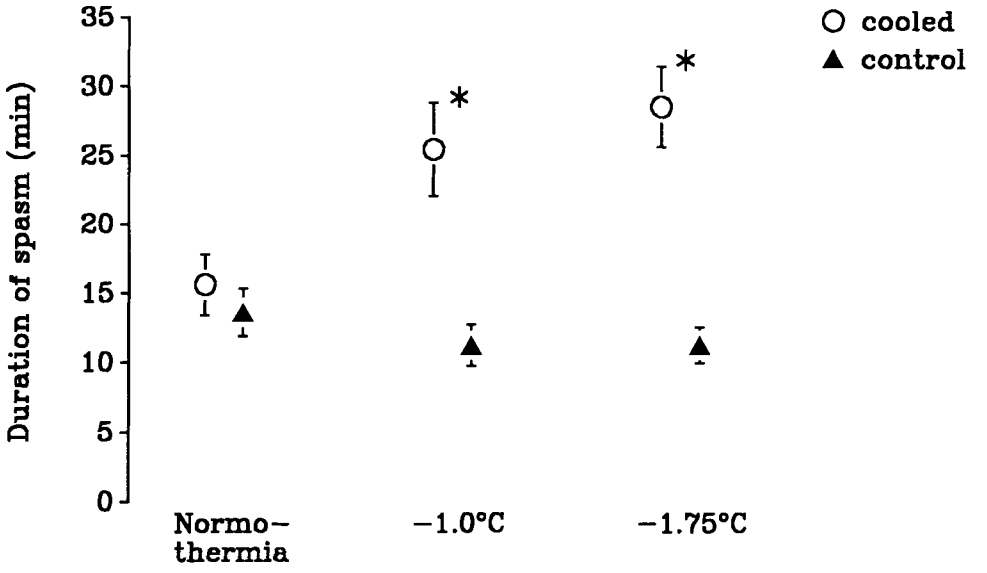

Fig. 7. The duration of spasm. The body temperature in the cooled group was reduced by close to 1.0 and 1.75°C in experiment 2 and 3, respectively. The control group was kept normothermic in all three experiments. N=5 in all experiments.

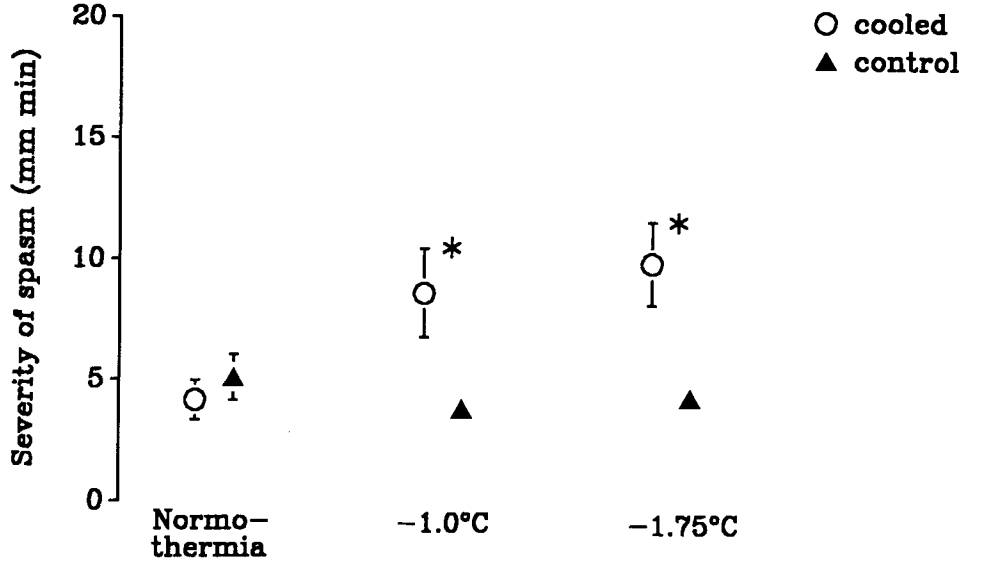

Fig. 8. The severity of spasm. The body temperature in the cooled group was reduced by close to 1.0 and 1.75°C in experiments 2 and 3, respectively. The control group was kept normothermic in all three experiments. N=5 in all experiments.

DISCUSSION

In this study we have shown that general hypothermia aggravates traumatic vasospasm in the central ear artery of the rabbit. It has been postulated on theoretical grounds that the rabbit ear is a specialized organ for temperature control (15,14). This has been studied specifically by Hill et al. (6), who found, however, that at low ambient temperatures there was a net heat loss, and that at high temperatures there was a net heat influx, demonstrating that the rabbit ear is not a special organ for temperature control. We therefore believe that the results of our studies on the rabbit ear artery can be generalized to most vascular beds.

There are several possible ways in which the body temperature might influence the duration and severity of vasospasm. Vessel contraction induced by reduction of the core and local temperature is known to be under sympathetic control (4,12,17,9). Thermodynamic studies of the noradrenaline receptor binding have shown a higher affinity for the receptor at lower temperatures (11) and that the maximal response to adrenaline and noradrenaline in the rabbit ear artery occurs at a temperature close to 25°C (8). There is also an increase in the myogenic tone, which is temperature-dependent. This latter increase seems to be independent of the adrenergic response but is Ca^{2+} dependent (5,3). These and other mechanisms may contribute to the aggravated response of traumatically induced vasospasm observed in the present study. Since the initial diameters of the vessels were similar at normal and reduced core temperature and since the serum cortisol levels remained unchanged, activation of the sympathetic response is probably not sufficient to explain the results. It is therefore possible that the myogenic temperature dependence is an important mechanism underlying the aggravation. This question cannot be answered with certainty, however, on the basis of our results. However, the present study has unequivocally shown that even a very small reduction of the core temperature aggravates traumatically induced vasospasm. This stresses the importance of careful control of the body temperature in clinical microsurgery.

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REFERENCES

1. Asp, C., Cox, R.G., Mayou, B.J. & Sengupta, R.: The role of anaesthetic management in enhancing peripheral blood flow in patients undergoing free flap transfer. Ann. R. Coll. Surg. 67:177, 1985

2. Bird, T. M. & Strunin, L.: Anaesthetic considerations for microsurgical repair of limbs. Can. Anaesth. Soc. 31:51, 1984

3. Bevan, J. A.: Vascular myogenic or stretch-dependent tone. J. Cardiovasc. Pharmacol. 7 (supp 3):S129, 1985

4. Grant, R. T.: Further observations on the vessels and nerves of the rabbit ear, with special reference to the effects of denervation. Clin. Sic. 2:1, 1935.

5. Harker, C. T. & Vanhoutte, P. M.: Cooling the central ear artery of the rabbit:Adrenergic Responses. J. Pharmacol. Exp. Therapeut. 245:89, 1988

6. Hill, R.W. & Veght, J. H.: Jackrabbit Ears: Surface temperatures and vascular responses. Science. 194:436, 1976

7. McDonald, D.J.F.: Anaesthesia for microvascular surgery. Br. J. Anaesth. 57:904, 1985

8. Patton, N. J. & Wallace, W. F. M.: Responses of isolated rabbit ear arteries to intra- and extraluminal L- and D-noradrenaline, L-adrenaline and histamine in the temperature range 37-3 °C. Irish J. Med. Sci. 147:313, 1978

9. Phelbes, D. B., Rutherford, R. B. & Boswick, J. A.: Control of vasospasm following trauma and microvascular surgery. 4:109, 1979

10. Pucket, C.L., Winters, R.R.W., Greter, R.K. & Goebel, D.: Studies of pathologic vasoconstriction (vasospasm) in microvascular surgery. J. Hand. Surg. 10A:343, 1985

11. Raffa, R. B., Aceto, J. F. & Tallarida, R.J.: Measurement of thermodynamic parameters for norepinephrine contraction of isolated rabbit thoracic aorta. J Pharmacol. Exp. Therapeut. 235:596, 1985

12. Riedel, W., Iriki. M. & Simon, E.: Regional differentiation of sympathetic activity during peripheral heating and cooling in anesthetized rabbits. Pfluegers Arch. 332:239, 1972

13. Robins, D.W.: The anaesthetic management of patients undergoing free flap transfer. Br. J. Plast. Surg. 36:231, 1983

14. Schmidt-Nielsen, K.: Desert animals. London. Oxford Univ. Press, 1964, pp. 133-38

15. Schmidt-Nielsen, K., Dawson, T. J., Hammel, H. T., Hinds, D. & Jackson, D.C.: The jack rabbit- a study in desert survival. Hvalrådets Skr. 48:125, 1965

16. Shaw, W.W. & Hidalgo, D.A.: Microsurgery in trauma. New York. Futura Publishing Company, Inc., 1987, p. 39

17. Walther, O. E., Iriki, M. & Simon, E.: Antagonistic changes of blood flow and sympathetic activity in different vascular beds following central thermal stimulation. Pflugers Arch. 319:162, 1970

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