Experimental Studies on the Hemodynamics of Spinal Cord in the Dog

by

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Considerable amount of works has been made on the circulatory disturbance of the brain, while little has been reported on the same subject of the spinal cord.

Less analytical attention has been paid to the spinal cord partly because (1) its pathology is less distinctly understood than that of the brain, (2) there is less opportunity of autopsy study on the spinal cord, (3) angiographic study is not of practical use, and (4) analysis of the clinical picture in relation to the circulation is difficult because of diversity and complexity of the vascular pattern.

Despite these reasons, detailed investigation of the vascular problems has become a matter of serious interest from the clinicopathological stand-point, particularly in the light of development of surgery on the aorta cast upon the increase of spinal cord injury as well as upon such diseases as cervical spondylosis and spinal arachnitis.

It seems well established that very little contraction of cerebral vessels takes place as a result of neural mechanisms.[1)2)3)]

On the other hand, it is now clear that spasm of pial vessels over the cerebral convexities and large arteries of the brain in animals does occur after local mechanical stimulation.[4)5)6)]

FIELD et al.,[7)] using a thermocouple, reported that blood pressure changes may produce passive response in the blood flow in the spinal cord in debilitated animals (rabbits). In fresh preparation, however, the blood flow in the spinal cord is largely independent of general blood pressure changes. Adrenaline was found to have a definite vasoconstrictor action on the vessels of the spinal cord.

OTOMO et al.[8)] made visual observation of pial vessels and polarographic measurement of oxygen tension in spinal cord, and concluded that chief factor controlling blood flow and oxygen tension of central nervous system is the systemic blood pressure. Control of blood flow by changes in diameter of superficial blood vessels is not observed.

The present study has been directed to an evalution of influences of sympathetic denervation on blood circulation in the spinal cord. Alteration of blood flow and pressure of several arteries which irrigate the spinal cord has been observed following sympathectomy. To register the effect of sympathetic denervation, temperature and oxygen availability in the spinal cord were measured. In order to avoid such artefacts as heat production by contraction of the neighboring muscles or fluctuation of oxygen availability caused by respiratory changes, the animals were given small doses of succinyl choline chloride (S.

C. C.) and placed on artificial respiration.

MATERIALS AND METHODS

The observations have been made on 40 adult mongrel dogs weighing 7 to 14 kilograms. All animals were anesthetized with intravenous pentobarbital (Nembutal) 25 mg per kilogram of body weight and small doses of S. C. C. were administered. Respiratory exchange was controlled by a mechanical respirator connected to the tracheal cannula.

Cervical, thoracic and lumbar laminectomies were performed for measuring temperature and oxygen availability in the spinal cord, each exposing about 5 to 7 mm of the spinal cord segment.

Stellate, upper thoracic (S-T4) and midthoracic (T6-T11) sympathectomies of both sides were performed via bilateral thoracotomies in the 2nd and the 6th intercostal space respectively. Bilateral lumbar sympathetic ganglions (L2-L6) were dissected and removed through abdominal approach.

Blood pressure was recorded continously by a strain gauge manometer connected to catheters which were inserted into the vertebral and femoral arteries. Flo-probes with the internal diameters of 1.5 mm and 4 mm were applied to the other vertebral and femoral arteries respectively and connected to an electromagnetic flowmeter (MEDICON). Tissue oxygen availability was determined with a physiological gas analyser (BECKMAN) using microelectrode. The animal was insulated and grounded from a point near the probes or O_2-electrode. Tissue temperature was monitored with thermisto-thermometer (SHIBAURA DENSHI) using 4 needle electrodes which were inserted into the subarachnoid space through laminectomy.

Room temperature was maintained at 20°-22°C.

RESULTS AND EVALUATIONS

Part 1

This experiment was carried out in order to observe the blood flow and pressure of the vertebral and femoral arteries following sympathectomy at various levels.

Results—Combined bilateral stellate and upper thoracic sympathectomy resulted in definite increase of flow rate and equivocal changes of blood pressure of the vertebral artery in most occasions, whereas there were no appreciable changes in the flow rate and blood pressure of the femoral artery. The flow rate of the vertebral artery increased to 120% of the resting level in 60 minutes after operation (Fig. 1).

Lumbar sympathectomy, on the other hand, was followed by a definite increase in the flow rate and equivocal changes in the pressure of the femoral artery, but not by a flow rate increase of the vertebral artery (Fig. 2).

Comment—The fact presented here that the combined removal of the stellate and upper thoracic sympathetic ganglions caused an increase in the flow rate of the proximal vertebral artery where the measurement was done. There also is a known fact that the distal vertebral artery gives flow, besides to the central nervous system, to the collaterals to cervical muscles in dog. Therefore increased flow in the proximal vertebral artery may not immediately mean increase of the flow in the central nervous system of vertebral distribution, but possibility still exists that increased flow rate of the proximal vertebral

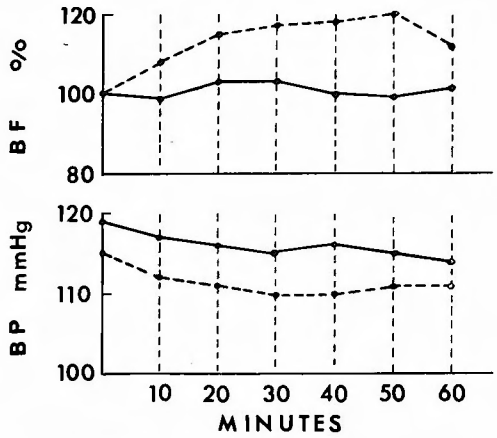

Fig. 1 Blood flow and blood pressure of vertebral (dottedline) and femoral artery (solid line) following combined stellate and upper thoracic sympathectomy. Each line shows average value of 4-5 dogs. Flow rate is expressed as per cent of initial value.

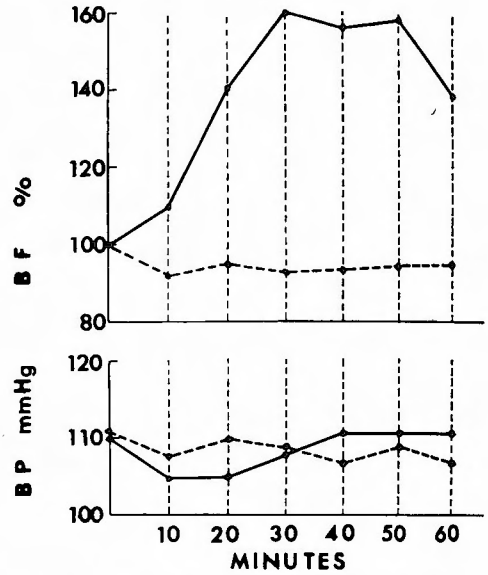

Fig. 2 Blood flow and blood pressure of vertebral (dotted line) and femoral artery (solid line) following lumbar sympathectomy. Each line shows average value of 4-5 dogs. Flow rate is expressed as per cent of initial value.

artery due to the removal of these ganglions will increase the blood circulation in the cervical cord. The lumbar cord is supplied by branches of the lumbar arteries, whereas, the femoral artery supplies muscles and skin of the lower extremity. Behavior, particularly the response to the vasomotor control may or may not be different between lumbar and femoral arteries. Thus, if not identically, there is a possibility, at least, of these vessels to behave in a similar fashion. Therefore an increase in the flow rate of the femoral artery following lumbar sympathectomy may suggest that the circulation in the area of the lumbar cord is also increased, although such analogy must be considered carefully.

Part 2

Possibility of improving the spinal cord circulation by sympathectomy was suggested in the foregoing experiment. The current experiment was undertaken with the purpose of measurement of temperature of the spinal cord after sympathectomy as an indicator of local circulation.

Laminectomy was performed at 3 or 4 different sites on each animal. Temperature was measured by a thermisto-thermometer using needle thermisters applied on the skin of extremities and on the exposed segments of the spinal cord. Following sympathectomy, temperature difference between the skin and the spinal cord at various sites was plotted. When the combined stellate and upper thoracic sympathectomy as well as the midthoracic sympathectomy was done, the skin temperature was measured at the proxymal part of a hind limb, while when the lumbar sympathectomy was done, it was taken from the skin at the proximal part of a forelimb. Respective temperature after the sympathectomy was compared with the temperature of the spinal cord exposed at various sites.

Room temperature was maintained at 20°-22°C during experiment.

Results—Even in the control animals which underwent laminectomy only, both skin and cord temperature dropped gradually about 4°-5°C in 90 minutes after operation and then fell further down. It is noted that grade of the fall of temperature is essentially parallel between the skin and the cord during and after operation.

Following combined bilateral stellate and upper thoracic sympathectomy (S-T4), grade of the fall of temperature is less at the cervical cord by 0.5°C in 90 minutes after operation as compared to that at thoracic and lumbar segments, temperature of latter two and of the skin of the hind limb being falling in parallel (Fig. 3).

Cases of the bilateral midthoracic sympathectomy (T6-T11) revealed less fall of temperature in a similar fashion selectively at thoracic segment of the cord, especially at its lower portion, as compared to the other part of the spinal cord (Fig. 4).

Also the similar principle applies in cases of the lumbar sympathectomy in which the

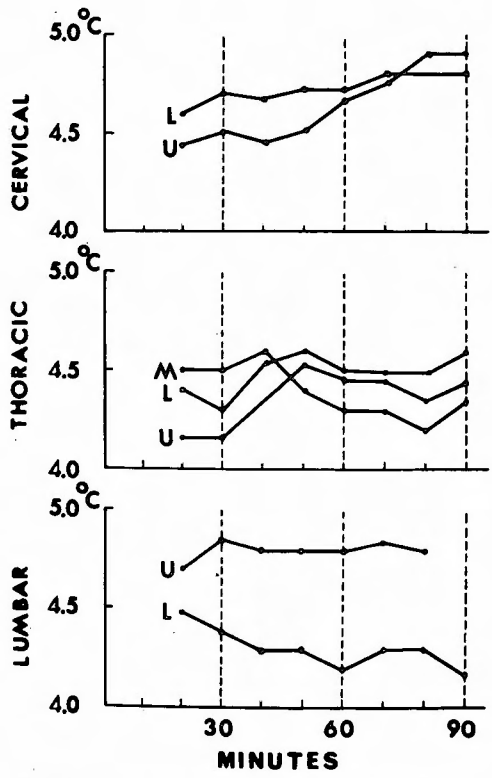

Fig. 3 Temperature-difference between spinal cord and skin of hind limb following combined stellate and upper thoracic sympathectomy. Each line shows average value of 4-5 dogs. U : upper, M : middle, L : lower portion of cord.

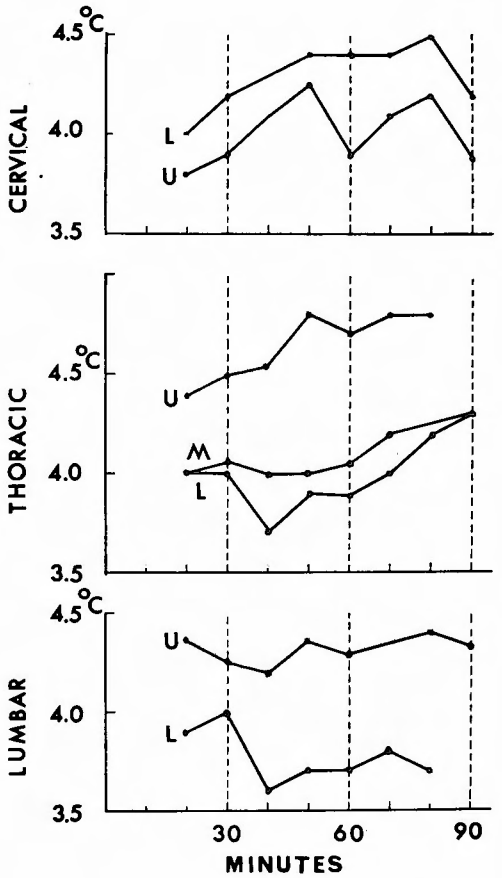

Fig. 4 Temperature-difference between spinal cord and skin of forelimb following midthoracic sympathectomy. Each line shows average value of 4-5 dogs. U : upper, M : middle, L : lower portion of cord.

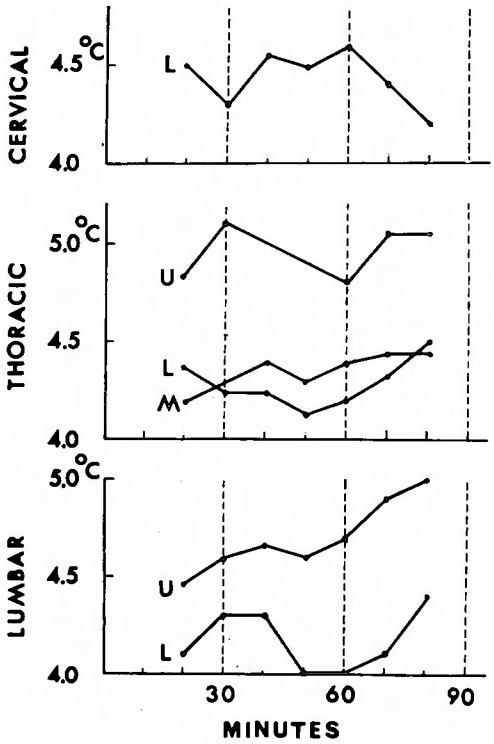

Fig. 5 Temperature-difference between spinal cord and skin of forelimb following lumbar sympathectomy. Each line shows average value of 4-5 dogs. U : upper, M : middle, L : lower portion of cord.

lower thoracic and lumbar segments revealed less fall of temperature than the rest of the cord (Fig. 5).

Comment—Although tissue temprature might not be considered directly indicative, it can be an indirect reflector of the state of local circulation. Since it is not possible to measure directly the flow rate of the vessel which supplies the spinal cord, the temperature measurement is employed in the current study as an only means to learn the state of local circulation.

On the basis of such postulation, this experimental result shows that sympathectomy give certain influence upon the spinal cord circulation. Thus combined stellate and upper thoracic, midthoracic and lumbar sympathectomies mainly affect the hemodynamics of cervical, thoracic and lumbar spinal segments respectively.

To be taken into account in this experiment, the condition of the animals thus prepared is always accompanied by the state of systemic hypotension. To the author's belief, this hypotensive condition as autonomic derangement state may contribute beneficially to the results of this experiment. As another additional condition to be taken into account, the effect of anesthesia may not be entirely neglected as regard to vascular response.

Part 3

It was confirmed that sympathectomy gives cirtain effects upon the spinal cord circulation in the previous experiments. Present study is to attempt to investigate the sympathetic influence upon the circulation in the lumbar segment of the spinal cord.

Sympathectomy at various levels was performed on the dogs, which was laminectomized beforehand at the level of the L 3 vertebra, and its effect on the oxygen availability and temperature of the lumbar cord was observed. The exposed portion of the cord was covered with a thin layer of mineral oil and was maintained thermically stable by mild heating.

Results—Oxygen availability of the lumbar cord under light anesthesia is within the range of 10-30 mmHg. In the control group which had only thoracotomy (which is a necessary preliminary for thoracic sympathectomy), oxygen availability of lumbar segment remained unchanged or slightly decreased, probably on account of operative procedures (Fig. 6A).

Combined stellate and T 4 sympathectomies were performed on 4 animals. Figure

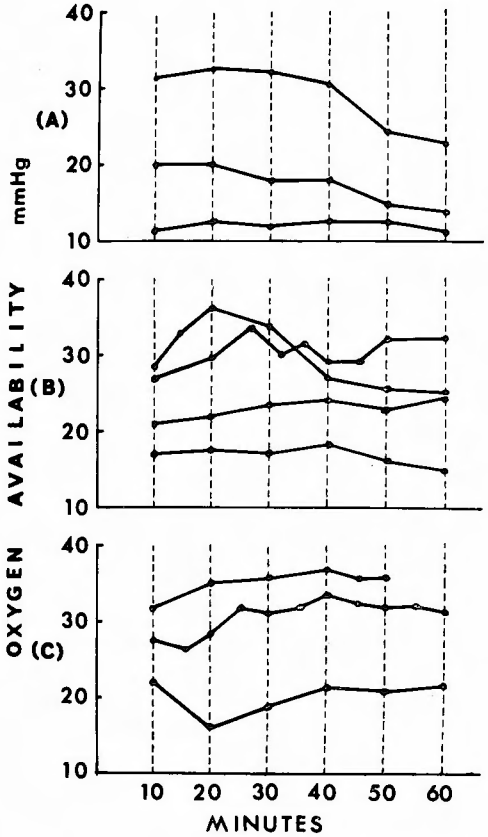

Fig. 6 The effect of thoracotomy (A), combined stellate and upper thoracic sympathectomy (B) and lumbar sympathectomy (C) upon oxygen availability of lumbar cord.

7 shows typical example of post-operative changes in oxygen availability, recorded from the lumbar segment. Oxygen availability increases gradually during the period of 40 minutes after the operation, and then either decreases slightly or remains unchanged (Fig. 6 B).

In 3 animals which received midthoracic sympathectomy (T 6-T 11), oxygen availability increased also slightly after the operation.

Lumbar sympathectomy produced mild to moderate increase in oxygen availability in the lumbar cord in 3 dogs (Fig. 6 C).

Comment—Although various methods for the investigation of peripheral circulation have been proposed, the ideal method has not yet been found. According to Meyer[9], if local tissue metabolism and the oxygen concentration in the general circulation remain constant, changes in local oxygen availability reflect alterations in local blood flow, and under light anesthesia, tissue metabolism and systemic oxygen concentration remain remarkably constant. In this experiment therefore, changes in local oxygen availability are considered an indicator of local blood flow. Polarographic measurement is employed for this purpose, because, not like temperature measurement, it can record values instantly as well as at closely situated spots.

The current between electrodes at given potential depends largely on the permeability of the membrane material of the electrodes and the permeability varies considerably with temperature change. Electrode sensitivity increases logarithmically as temperature rises. Figure 6 shows the corrected PO_2 values according to the temperature-coefficient.

Otomo et al.[8] made polarographic observations of oxygen tension of the cord following administration of various drugs, and showed that systemic blood pressure brought about passive responses in the blood flow in the spinal cord. Figure 7 shows that following

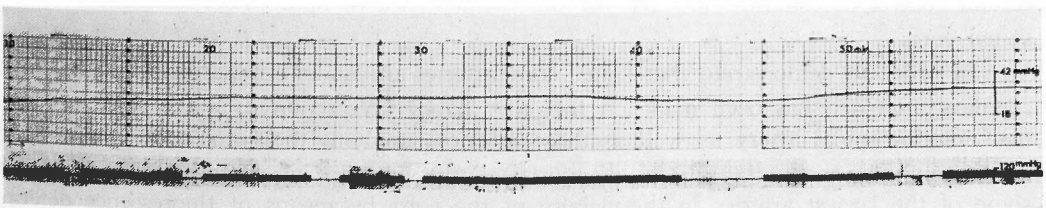

Fig. 7 The oxygn availability of lumbar cord and the blood pressure of femoral artery following combined stellate and upper thoracic sympathectomy.

sympathectomy, oxygen availability of the cord is elevated slightly without concomitant rise in the systemic blood pressure.

DISCUSSION

It is generally known that both intracranial pial and intracerebral arteries are supplied with nerves.[10)11)12)] Similar observation was reported with regard to pial vessels of the spinal cord by CLARK.[13)]

While vessels of the skin of ear contract 80 per cent upon stimulation of the cervical sympathetic nerves,[14)] pial vessels over cerebral convexity of cats do not constrict more than 3 to 18 per cent of their initial diameters.[15)] The blood flow of internal carotid artery in monkeys decreases about 30 per cent by stimulation of the cervical sympathetic nerves without involving contamination of the blood flow of external carotid artery.[16)]

Many clinical conditions such as convulsion, migraine, transient cerebral ischemic attack have been interpreted as manifestations of cerebral vasomotor phenomena. And stellate block has been granted as one of the effective treatments for vasospasm, embolism or thrombosis of cerebral vessels.[17)18)19)]

On the other hand, there are numerous contradictory evidences that this procedure has no effect on cerebral blood flow and circulatory resistance.[20)21)22)]

To the author's experience, the autonomic response seems to be evoked effectively only under its deranged state. It is believed, in relation to the results, that the hypotensive state as a result of surgical insult for the preparation of the animals is a manifestation of autonomic derangement which, in turn, has contributed beneficially in order to obtain demonstrable response to those given experimental conditions applied to the sympathetic nervous system.

Although many investigators corraborate that cerebral and spinal cord circulation is considerably subject to the systemic blood pressure even under light anesthesia, some control mechanisms are assumed to work in order to keep the circulation through the central nervous system stable against physiological or pathological alterations of systemic blood pressure. Vasomotor control, howmuch-ever it may, is assumed to play some role in circulatory regulation of the central nervous system especially under pathological condition such as hypotensive state.

The spinal cord receives several arteries directly from aorta. Therefore, the spinal cord circulation would be under direct influence of the systemic hemodynamics, if there be no control mechanism to secure adequate circulation for the spinal cord. Actually, as a part of the spinal cord is activated, the local circulation of that part will be augumented to meet requirement.[23)] This thought, in consideration of afore-mentioned, leads us assume certain control mechanisms to exist for the maintenance of appropriate circulation for the spinal cord.

In order to demonstrate that spinal cord arteries are under adrenergic influence, histochemical approach has been made on the other hand. We reported, in the separate paper, that anterior spinal artery as well as those arteries supplying the spinal cord present MAO activity in their media.[24)] FALCK demonstrated the presence of adrenergic innervation in some of the largest arteries in the vicinity of the cord, by means of fluorescence determination of cathecholamines.[25)]

It is found in Part 2 that cervical, thoracic and lumbar sympathectomies give some influence upon the circulation of corresponding spinal cord segments. Moreover, the lumbar cord circulation is influenced not only by the lumbar sympathetic ganglion but also by the stellate as well as upper thoracic ganglion, as revealed by the Part 3 experiments. Therefore, thus, the lumbar sympathetic ganglion is not only affector of the lumbar cord circulation. In other words, the lumbar cord circulation is modified also by some other affectors, beside the lumbar sympathetic ganglion.

In accordance with this view, it is our experience that noradrenaline does not completely disappear following lumbar sympathectomy from the anterior spinal artery at the lumbar segment, whereas it does completely so from the dorsal pedal artery.[24] Thus, the circulation of the lumbar segment of the spinal cord is affected not solely by the lumbar sympathetic ganglion.

STRICKER reported a case of meningioma of the upper thoracic segment, which, although having been treated with the complete removal of the tumor and lumbar sympathectomy, suffered from postoperative persistence of intense pain and cramps in the calves and thighs.[26] These complaints were completely cleared by the additional upper thoracic sympathectomy. He postulated that prolonged vasospasm, which might eventually bring about serious pathological disorders, but that their effects were reversible after long periods of ischemia, was caused by the mechanical pressure and irritation of the tumor and this vasospasm was released following the addition of the upper thoracic sympathectomy.

We have experienced several cases of "non specific,, encephalomyelitis with sensori-motor disturbances of the lower extremities. Their clinical pictures improved remarkably following either block or resection of the upper thoracic segments.[27] The mechanism of the benificial effect is not entirely clear, but at least the improvement of circulation of the spinal cord as a result of the sympathetic denervation seems to have played an important role.

SUMMARY

The following experiments were performed on 40 dogs to elucidate the influence of sympathetic nervous system upon the circulation of spinal cord.

Alterations following sympathectomy of the blood flow and pressure of several arteries which irrigate the spinal cord have been observed. To register the effect of sympathetic denervation, temperature and PO_2 at various sites in the spinal cord were measured.

1) Circulatory resistance of the vertebral and femoral arteries decreased following combined stellate and upper thoracic, and lumbar sympathectomies correspondingly.

2) Combined stellate and upper thoracic, midthoracic and lumbar sympathectomies mainly give certain influence upon the temperature of the cervical, thoracic and lumbar segments respectively.

3) The circulation of the lumbar segment of the spinal cord is affected not solely by the lumbar sympathetic ganglions, but also by the sympathetic ganglion of higher level, or possibly by some other mechanisms in addition.

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和文抄録

犬脊髄の血行動態に関する実験的研究

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中枢神経系の血管性障害に関する研究のうち，脊髄に関するものは，脳に比べて極めて少なく，この分野における研究が，おくれていることに著目し，成犬を用いて，脊髄の血行動態に関する研究を行なつた．

中枢神経系の血液循環に関する神経性調整因子の関与は，身体の他の部分に比べて微弱であるとされている．著者は，犬脊髄の血液循環について，交感神経切除術が及ぼす影響について，脊髄流入血管の血圧及び血流量，脊髄の組織酸素濃度及び温度を測定することにより観察した．実験は原則として筋弛緩剤を用いて，調節呼吸下に行なつた．

（1） 星状及び上胸部交感神経節切除により，椎骨動脈の循環抵抗は減少するが，大腿動脈では著変をみない．腰部交感神経節切除により，大腿動脈の循環抵抗は減少するが，椎骨動脈では著変をみない．これらの動脈の循環抵抗の減少は，中枢神経系，殊に脊髄への血流量増加を直接意味するものではない．

（2） 星状及び上胸部交感神経節切除は主として頸髄の，腰部交感神経節切除は主として腰髄の局所温度の相対的上昇を来たす．この際，動物は椎弓切除及び開胸操作のため，出血性低血圧下にあり，これは，結果的に交感神経緊張状態を惹起したものと考えられる．

（3） 腰髄の局所酸素分圧は，腰部交感神経節切除のみならず，上胸部交感神経節切除によつても影響される．したがつて，腰髄の血液循環は，当該交感神経節のみならず，高位交感神経節及び他の血流調整機転の関与を受けるものと推察される．

（4） 以上の知見より，臨床的にも，脊髄の血行障害に対して，交感神経節切除を試みることは意義あるものと考えられる．