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A Critical Study of The Cold Pressor Test (1)

THE INFLUENCE OF THE ARACHNOIDITIS SPINALIS ON THE COLD PRESSOR TEST

BY

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CHAPTER 1 INTRODUCTION

The cold pressor test (C. P. T.) was first presented by Hines and Brown⁸⁾, 1932 together with standard method of giving cold stimulus, and it was shown that the reaction has two types, hyper-reacter type and hypo-reacter type.

I) COLD PAIN

A cold stimulus to the skin gives rise to a cold sensation, puls, after the lapse of certain time, a peculiar sensation of pain. This pain is called "Cold Pain". This pain is generally ascribed to a direction action of the given stimulus on the vascular wall.

In this communication it will be disclosed, that degree of a cold pain depend upon the excitability of the local blood vessel; namely, local blood vessel in the state of constriction elicits a weak cold pain, hence weak pressor effect, while local blood vessel in the state of dilatation elicits a strong cold pain, hence strong cold pressor effect. From this view point further, the author will discuss the influence of arachnoiditis on the C. P. T.

A) Characteristics of the cold pain

Wolf and Hardy¹⁸⁾ (1941) stated as follows, regarding the cold pain.

- 1) Cold pain is entirely separate from and independent of the sensation of cold itself.
- 2) This type of pain does not show the phenomenon of spatial summation since exposure of one finger to cold causes pain of equal intensity to that experienced when the whole hand is so exposed.
- 3) The pain may be induced on nearly all parts of the body. In each case the highest bath temperature at which pain can be obtained is 18°C.
- 4) The skin temperature of the immersed part decreased rapidly for the first minute after immersion and then much more slowly.
- 5) The amplitude of pulsation of the digital

artery parallels inversely the intensity of "cold pain" experienced.

- 6) The blood pressure-raising effect is proportional both to the intensity of pain experienced and to the degree of cold.
- 7) Ischemia, which is known to produce pain in muscular structures, is not a significant factor in the production of "cold pain".
- 8) By selective partial block of nerve trunks, it was indicated that "cold pain" is carried by the small, non-myelinated fibers of class C.
- 9) Sympathectomy was found to augment the intensity of pain derived from cold.
- 10) It was found possible to lower the bath temperature to zero without pain being felt in the immersed hand if the cooling were carried out slowly enough.
- 11) By successively cooling different parts it was learned that the production of "cold pain" depends on local changes in the part cooled.
- 12) Evidence is presented which indicates that the elevation of blood pressure which results from immersion of a part in cold water is a measure of the subject's reaction to "cold pain".

B) Cold pain and sympathetic tone

1) Liwingston⁴⁾ (1930) stated as follows, regarding the relation of the vasoconstrictiveness to the extrinsic nerve.

The blood vessels are thus seem to possess an autonomy of function very similar to that displayed by the gastro-intestinal tract after it has been deprived of its extrinsic nerves.

This autonomy and the coordinating function of the extrinsic nerves to blood vessels is well illustrated by Cannon's sympathectomized cats. These animals, from which Cannon had removed the entire peripheral portion of the sympathetic nervous system, maintained an apparently normal circulation under favorable environment, but were

extremely sensitive to cold.

Cannon attributed their sensitiveness to cold, in part at least, to the animal's inability to reduce the peripheral circulation in the normal manner.

2) In 1941, Wolf and Hardy¹⁸⁾ described the effect of sympathectomy on C. P. T. as follows:

In order to determine any possible influence of these upon the phenomenon of "cold pain", a patient who had had the cervical sympathetic ganglia on the right removed within the previous four weeks for intractable asthma was used as a subject.

It was found that his right hand was markedly warmer than his left. The completeness of sympathectomy was demonstrated by comparing the change in skin resistance in the two hands upon the application of nociceptive stimulus. Repeatedly there was a marked change in resistance on the left and none at all on the right. When the left arm was immersed in cold water, the usual cycle of pain and blood pressure elevation occurred. When the right hand was immersed, however, the pain was much more severe and the elevation of blood pressure much more marked. At 10°C, for example, there was a diastolic rise of 10 mmHg when the left arm was immersed and 20 mm of Hg when the right arm was immersed. When the circulation to the arm was interrupted by a sphygmomanometer cuff, the effect were not altered.

3) According to Reiser and Ferris²⁴⁾, 1948, who performed C. P. T. following the intravenous administration of T. E. A. C. in doses of 500 mg, one patient subjected to this experiment experienced severe cold pain and yelled agonizing cry, exhibiting an abrupt elevation of the blood pressure of over ten minutes' duration after the cessation of the stimulus, while eleven patients experienced similar cold pain, though milder in degree. They attributed such elevation of the blood pressure to the action of some humoral substance, Epinephrine for instance, since the elevation occurred during the T. E. A. C. administration.

The above cited work of various authors indicates that when a C. P. T. is instituted, an usual cold stimulus evokes a greatly enhanced vascular response from a locality where sympathetic nerve excitability is being lowered, and for this reason, it elicits a severe cold pain.

Then, what about the case where sympathetic nerve is being excited?

4) In 1941, Himmelsbach¹⁹⁾ studied the effect

of C. P. T., administering sympathicomimetic drug as follows: With 20 mg. of Benzedrine subcutaneous, pressor response was lowered; with 0.2 mg. of Epinephrine subcutaneous, there was normal pressor response; with 2 mg. of Strichinin subcutaneous, there was lowered pressor response.

5) Dieckmann and Michel⁶⁾, 1935, studied C. P. T. in pregnant women.

Their observation on 40 pregnant women with temporary hypertension associated with eclampsia disclosed that C. P. T. in such condition was that of elevation of systolic pressure by 26 mmHg in average, not much different from the normally encountered pressor response in healthy individuals. Why this is so, they explain as follows:

The relatively small increases in systolic pressure in the eclamptic and preeclamptic groups afford an opportunity for speculation and conjecture.

Apparently in these patients the vascular spasm is at its maximum or there is a diminished response to pain stimuli.

This has been demonstrated by Spiegler and Schol, who found that eclamptic patients required a greater cathodal closing current to elicit a contraction than did normal pregnant women. (*Die Galvanische Nerven-Muskelerregbarkeit In Der Schwangerschaft Und Bei Toxikosen. Arch. f. Gynak.* 1930)

The above experiment indicates that, in an individual whose sympathetic excitability is being enhanced so that his blood vessel is already in the state of vasoconstriction, a cold stimulus does not cause further vasoconstriction, hence there is only feeble cold pain.

6) Thirty cases of essential hypertension were studied by Matsushita³²⁾, Nara University, 1955, who performed C. P. T. and measurement of Total Renal Resistance at the same time. He disclosed that decrease of R. P. F. during C. P. T. was minimal in magnitude in those whose Renal Plasma Flow at rest was small, that some patient with R. P. F. smaller than 190 cc/min at rest even exhibited an increase in R. P. F. during the institution of C. P. T.. This implies that spastic blood vessels are revealed by decreased R. P. F. are not very responsive to a cold stimulus, or beyond certain degree of spastic vasoconstriction, they even respond in inverse manner to a stimulus. Inverse response of the excessively constrictive blood vessel, namely its dilatation upon application of cold stimulus, with consequent depressor effect, has been given some

supporting evidence by the following work of Igersheimer²⁶).

He disclosed that the cold pressor response in psychotic patients, who are off balance of the autonomic nerve tone, was extremely poor in showing elevation of the blood pressure, response being often of inverse type in severe cases.

7) Regarding the relation between the autonomic imbalance and C. P. T., Igersheimer presented the following experiment in his "C. P. T. in Functional Psychiatric Syndromes", 1953.

An inter-group comparison of normal, psychoneurotic, schizophrenic, and manic-depressive subjects using the cold pressor test of Hines and Brown was made. Statistically significant difference were observed between the normal and the schizophrenic group. The group of psychoneurotic patients seemed to occupy an intermediate position between the normal and the psychotic group with regard to the cold pressor responses.

The significantly lower cold pressor responses in the schizophrenic and manic-depressive subjects were related to Gellhorn's theory of deficient reactivity of the sympathetic division of the hypothalamus in the functional psychoses, particularly in schizophrenia. A hypothalamic depressor mechanism governing lower vasomotor center is suggested.

"Paradoxical" cold pressor responses found in five schizophrenic subjects were interpreted according

to Gellhorn's theories, emphasizing that the vagal-parasympathetic centers may be unusually hyper-reactive to cold stimulation in these subjects. Allusion is made to the possibility that this response may be due largely to a depressor effect exerted by the hypothalamus over lower vasomotor centers.

Summarizing the above cited work of various authors, it is indicated that in C. P. T. the degree of the pressor effect is determined by the intensity of cold pain, and this cold pain, in turn, is determined by the exciting state of the blood vessel in locality where the cold stimulus is applied,—weak cold pain being elicited from spastic blood vessel and strong cold pain being elicited from dilating blood vessel. Degree of the vasoconstriction or vasodilatation is determined, of course, by the innervating autonomic nerves, therefore, it is very possible that the state of the spinal cord, or whether it is in pathologic excitation or not, has an important bearing on the pressor response of the individual.

II) RELATION BETWEEN SENSORY DISTURBANCE AND VASOCONSTRICTOR-RESPONSE

The relation between sensory disturbance, hyperesthesia or hypesthesia, and vasoconstrictor-response was studied by Marquis and Williams¹⁴), 1938, who employed pin-prick and cold as the method whereby to give stimulus. For recording vasoconstrictor-response, a small glass plethysmograph was sealed to finger or toe by means of zinc

Case	Diagnosis	Level of lesion	Direction of sensory change	Stimulus	Normal resion	Affected resion	Difference
1.	Areas of hypo and hyperaesthesia due to involvement of a peripheral nerve in scar tissue.	Peripheral	Hyperaesthesia	Strong P. P.	20.1 mm	36.0 mm	15.9
			Hypaesthesia	Strong P. P.	20.1 mm	15.1 mm	5.0
2A.	Hyperaesthesia due to involvement of peripheral nerve in scar tissue.	Peripheral	Hyperaesthesia	Strong P. P.	7.9 mm	17.9 mm	10.0
				Cold	7.4 mm	16.0 mm	8.6
2B.	Analgesia below D. 8. following subsequent chordotomy.	Dorsal 8.	Analgesia	Strong P. P.	9.1 mm	2.2 mm	6.9
				Cold	12.3 mm	1.2 mm	11.1
3.	Post-herpetic hyperaesthesia.	Dorsal 5.	Hyperaesthesia	Strong P. P.	7.7 mm	15.3 mm	7.6
				Cold	2.3 mm	12.3 mm	10.0
4.	Hyperaesthesia due to a spinal cord lesion.	Lumbar	Hyperaesthesia	Strong P. P.	2.0 mm	9.1 mm	7.1
				Cold	2.3 mm	12.9 mm	10.6
5.	Hypaesthesia due to lesions of the spinal cord at C. 3 on the right, and D. 8 on the left.	Dorsal 8.	Hypaesthesia	Strong P. P.	8.7 mm	1.4 mm	6.3
				Cold	17.9 mm	2.5 mm	15.4
6.	Hyperaesthesia following spinal cord injury.	Dorsal 4-8.	Hyperaesthesia	Strong P. P.	5.9 mm	20.9 mm	15.0
				Cold	7.0 mm	27.2 mm	20.2
7.	Hypaesthesia due to spinal cord tumor	Cervical 2.	Hypaesthesia	Cold	12.8 mm	3.3 mm	9.5
By D. G. Marquis and D. J. Williams				1 mm deflection per 10 cm finger volume			

oxide paste, and the change in finger volume was recorded by continuous film camera.

The pin-prick stimulus was delivered by means of a modified Head algometer, with which the intensity could be varied by adding or removing weights. "Weak" pin-prick was normally perceived as sharp but not unpleasant; "strong" pin-prick was definitely painful and when applied without warning was apt to provoke retraction of the part stimulated.

Temperature stimuli were obtained by the application of flat-bottomed copper calorimeter, 5 cm in diameter, which were filled with water of measured temperature. Stimuli designated as "hot" were between 45°C and 50°C: the "cold" stimuli were between 0°C and 10°C. Stimuli were applied to the patient in a predetermined random order at various points on the body in order to avoid any marked adaptation effects. Sufficient time elapsed between stimuli for the return to the basic dilated state.

The result of their study, as presented in the following table, indicated that there was increased responsiveness to pin-prick and cold stimulus where hyperesthesia existed.

As was revealed by case-3, cold stimulus to the Head's zone elicited markedly increased sympathetic response.

With above fact in mind, it appears highly probable that there will be enhanced vasoconstrictor response to cold stimulus in case spinal ganglia are in the state of excitement.

III) RELATION BETWEEN HYPER-REACTOR AND HYPERTENSION

It appears that there exists no such relation as that hypertensive subjects exhibit hyper-reactor type of cold response. According to the Study of Dickmann and Michel⁶⁾, eclamptic women developing hypertension exhibited decreased cold pressor response. In contrast, there is another report that hypertensive patients with nephritic toxemia showed very increased cold pressor response, the observed systolic elevation being 51 mmHg on an average for 30 individuals. (This report says that 5 patients among them showed side-effects such as hematuria after the institution of C. P. T.)

IV) AFFERENT PATH WAY IN THE COLD PRESSOR RESPONSE

In 1941 Wolf and Hardy¹⁸⁾ studied the effect on C. P. T. of compressing the arm tightly for 45

minutes to cause ischemia, and found that cold pain sense was retained even after the complete loss of touch, pain and warm sense, thus being able to produce a pressor effect. When Procain Hydrochloride, 1%, has been injected around the ulnar nerve in doses of 3 cc, subsequent C. P. T. dipping the 4th and 5th finger to the cold water, failed to evoke a cold pain, while, in this stage of anesthesia, touch, pain, warm and cold sense were kept intact.

Lewis and Pockin¹²⁾ reported in 1937 that in their experiment, where anesthesia was instituted in the presence of stationary blood stream, the large fiber of class A was the first to stop the transmission, while the smallest non-myelinated fiber of class C was the last to stop the conduction.

Gasser and Erlanger²⁾, 1929, reported that Cocain anesthesia blocks the smallest fiber of class C first, and the largest fiber of class A last.

The above experiments indicate that the cold pain conducted by the smallest fiber of class C, and it is independent of superficial sensation transmitted from the skin.

Marquis and Williams¹⁴⁾ reported in 1938 that the injury of the posterior root caused by a lesion to Cauda equina resulted in the absence of cold pressor response in the foot.

Sugi³⁴⁾ from Kyushu University noted, in his experiment on C. P. T. in the dog's rear legs employing Dry-ice, the disappearance of pressor response following the amputation of the sciatic nerve. He also found that the animal retains normal pressor response in the forelegs, but loses pressor response in the rear legs after its spinal cord has been amputated at the level of D₁₁—D₁₂.

Employing the vasogenic pain caused by the arterial injection of 5% Lactid acid, Buget and Livingston³⁾, 1931, produced elevation of blood pressure, and found that this pressor effect is transmitted centripetally by way of the posterior root fiber at the level of C₇, C₈, D₁, for the main part, and blocking this route results in the disappearance of the pressor effect.

Resection of the stellate ganglia and the 2nd thoracic ganglia blocked the pressor response completely, so it was suggested that the afferent pathway is similar to the somatic afferent fiber, entering the spinal cord through the port of posterior root.

With regard to its pathway in the spinal cord, Marquis and Williams¹⁴⁾, 1938, presented the follow-

ing report. They made C. P. T. in a patient who had a spinothalamic section performed at the level of the 8th thoracic segment, and found normal response on the healthy side, but complete block of response in leg on the side operated upon by spinothalamic section. They concluded that the Tr. spinothalamicus was the afferent pathway for the cold pressor response.

V) CENTER OF THE COLD PRESSOR RESPONSE

In 1929 Bard resected the cerebral hemisphere and dorsal thalamus in cat and applied stimulus to the periphery. Such cat was found capable of showing a pressor response.

Marquis and Williams¹⁴⁾ (1938) performed C. P. T. in patients with thalamus injury and found the same magnitude of pressor response on right and left. They concluded, therefore, that the arc of such vasomotor reflex is completed below the level of sensory thalamus, or in the brain stem.

According to Bronk, Pitt and Larrabe (1940), "The response to peripheral stimulation was not affected by removal of the hypothalamus. Under appropriate experimental conditions, however, stimulation of the hypothalamus was shown to cause the blood pressure to rise; Concomitant peripheral stimulation augmented this effect".

Sugi³⁴⁾ from the Kyushu University (1955) reported that the pressor phenomenon in C. P. T. was due to a reflex evoked by stimulus to the periphery with its center in the mid-brain, and that the direct mechanism for the elevation of blood pressure was the vasoconstriction in the splanchnic region without the involvement of the cardiac output.

VI) THE EFFERENT PATH OF THE COLD PRESSOR RESPONSE

Igerscheimer²⁶⁾ performed a C. P. T. on human body in 1953 under the intravenous administration of T. E. A. C. in doses of 500 mg. and found the pressor response completely blocked. Since T. E. A. C. acts on the sympathetic ganglia (Lyons, Moe, Neligh²³⁾, 1947), they concluded that a cold pressor response was probably due to some reflex. (In view of the fact that elevated blood pressure lasts over 10 minutes even after the cessation of C. P. T. in case it evoked severe cold pain, they concluded that such elevation of blood pressure was probably due to the discharge of Epinephrin under the administration of T. E. A. C.)

Sugi³⁴⁾ from Kyushu University (1955) per-

formed C. P. T. in dogs using dry-ice, and found that severing the spinal cord at the level of D₄—D₅ had the effect of blocking a pressor response either when stimulus was applied to the fore-limb or when given to the hind-limb. He also found that severing the brainstem between Pons and Diencephalon produced a blocking in pressor response, while it did not inhibit the animal to respond to Pikrotoxin and Adrenalin, that severing the splanchnic nerve on both sides resulted in marked decrease in pressor response and disappearance of the otherwise occurring elevation in blood level of sugar.

On the other hand, Igerscheimer²⁶⁾ observed the effect of spinal anesthesia on C. P. T. in men and found that spinal anesthesia reaching the level of D₄ (as caused by 100 mg. Procaine) blocked the C. P. T. in hand completely, while pressor response was restored when anesthetized region narrowed down to D₃.

With regard to the efferent pathway, Hines and Brown⁸⁾ found that a unilateral cervico-thoracolumbar-ganglionectomy failed to block a cold pressor response, while bilateral extirpation of D₇—D₁₂ sympathetic ganglia diminished the cold pressor response.

Takeuchi³³⁾, Inoue from Nara University studied C. P. T. after severing the splanchnic nerve unilaterally or bilaterally just below the diaphragm and found occasional positive pressor response even after the bilateral section. In such instances, they concluded, some sympathetic pathway other than the splanchnic nerve or some humoral factors should be involved.

In 1936 Bolton and Sturp⁹⁾ noted a decrease in digital pulse amplitude in extremities accompanying deep respiration, and found the afferent stimulus responsible to arise in the intercostal nerve. Their experiments indicated that resection of the Gangl. Stellatum or Plexus Brachialis could extinguish such decrease in pulse amplitude in hand, that lumbar-sympathetic ganglionectomy, and not a spinal injury below the level of L₁ could extinguish such decrease in pulse amplitude in leg.

In view of such work as cited above, the reflex arc responsible for a cold pressor response may be of such features as following;

a) The afferent pathway of the cold pressor response seems to begin with the smallest nervous fiber of class C around the vascular wall beneath

the skin, and ascends, through dorsal root fiber, to reach the corresponding spinal segment, and reach the hypothalamus by way of Tr. Spinothalamicus to switch to the efferent pathway. (Another postulation says that the afferent pathway does not enter the hypothalamus, but switches to its efferent fiber at the brain stem below sensory thalamus.)

b) The efferent pathway of the cold pressor response seems to descend through the spinal cord and terminate in the spinal sympathetic ganglia occurring between the 8th cervical and the 5th lumbar segment. The fibers arising here pass through sympathetic trunk to be distributed to the vascular wall of respective region. Therefore, it appears that a cold stimulus causes the blood vessels throughout the body to be constricted, but the chief blood vessels playing role being probably those of major splanchnic region.

VII) MAGNITUDE OF THE PRESSOR EFFECT IN THE COLD PRESSOR TEST

Hines¹⁷⁾ examined 1000 normotensive subjects for cold pressor response in 1940 and found 156 hyper-reacters and 859 hypo-reacters. Magnitude of the elevation of blood pressure was: systolic 31.2 mmHg and diastolic 27.5 mmHg in hyper-reacter, systolic 12.4 mmHg and diastolic 10.1 mmHg in hyporeacter.

Russek²¹⁾ examined 200 normotensive subjects for C. P. T. in 1934, and found 82 hyper-reacters with elevation in blood pressure of systolic 32.0 mmHg and diastolic 21.5 mmHg, while he found 118 hyporeacters with elevation of systolic 14.0 mmHg and diastolic 10.4 mmHg.

Matsushita³²⁾ from Nara University (1955) studied 10 normotensive subjects for C. P. T. in their soles, and found an elevation of blood pressure by 23 ± 15 mmHg in systolic and 9.5 ± 7 mmHg in diastolic blood pressure.

In view of above cited reports, average magnitude of the elevation in blood pressure during a cold pressor test seems to fall between 15 mmHg and 30 mmHg. It also appears that a completely "normal" subject should show equal magnitude of pressor response either when his foot sole has been stimulated or when his palm has been stimulated.

VIII) RELATION BETWEEN C. P. T. AND RENAL CLEARANCE

Takeuchi and Matsushita³²⁾ from Nara University performed C. P. T. on 10 healthy individuals and found a decrease by 24% in renal plasma flow

due to the performance of C. P. T..

The same authors performed C. P. T. at foot in 30 subjects with essential hypertension each for 10 minutes and similarly found decrease in renal plasma flow. Magnitude of the decrease was larger proportionately to the renal plasma flow at rest. Namely, subjects with over 431 cc/m of R. P. F. at rest showed a decrease by 23%, those with 430—300 cc/m of R. P. F. at rest showed a decrease by 9% and those with under 299 cc/m of R. P. F. showed no definite tendency, sometimes showing a slight decrease and sometimes increase.

As to the relation between the degree of R. P. F. decrease and that of pressor effect, the same authors reported that the two are not closely related to each other, individuals with marked pressor response exhibiting no outstanding decrease in R. P. F., and those with no great pressor response showing marked decrease in R. P. F.. They postulate that the constriction of renal arteries due to C. P. T. may be an expression of a generalized arteriolar constriction.

With regard to the problem of whether or not renal arteries in essential hypertension are more easily liable to spasm upon the arrival of a stress than are renal arteries in normal subjects, the same authors showed that the observed decrease in R. P. F. in essential hypertension ($23\% \pm 14\%$) was not significantly different from that of normal subjects ($25\% \pm 12\%$). It was also the case with total renal resistance. The authors concluded, therefore, that there was no evidence indicating that renal arteries are more sensitive to C. P. T. in essential hypertension than in normal subjects.

Dickmann and Michel⁶⁾ performed C. P. T. on 30 subjects with nephritic toxemia and found five of them extremely sensitive to the test, showing convulsion, hematuria, anuria, collapse, severe gastric pain, blindness and nausea after the test was over. One of them exhibited an elevation of blood pressure as great as over 60 mmHg till the 7th day when a venesection was made. (Cold stimulus had been given to the hand for one minutes.)

CHAPTER 2. PURPOSE OF THE PRESENT EXPERIMENT

At the meeting of the Japan Circulation Society, 1953 Maekawa from Kyoto University gave a report on hypertension to which subject he had been assigned. He postulated that an essential hypertension is ultimately due to a disturbance in A. T. P.

—A. T. P.-ase system, particularly the liberation into the blood stream of Kidney A. T. P.-ase. He pointed out, later, that the presence of subarachnoid adhesion, occurred in related spinal cord segments, plays an important role in the development of such disturbance.

This notion is based on the fact that hypertensive subjects show subarachnoid adhesion with high frequency at the level of the lower thoracic and upper lumbar segments. At this level of the spinal cord there exists the spinal sympathetic of T_{11} — L_1 , and continual stimuli arising in the subarachnoid adhesion results in a lasting excitement of the sympathetic nerve which leads to a renal ischemia. Such stimuli, arising outside of the spinal cord, do not injure the lateral horn, and, because of this fact, stimuli flow solely into the kidneys for a long period of time, and such lasting renal ischemia, as in the case of Goldblatt or Page's ischemic kidney, leads to a liberation of kidney A. T. P.-ase into the blood stream, hence a hypertension. Some subjects of essential hypertension, however, do not exhibit severe decrease in renal blood flow, and some show even an increased renal blood flow. In answer to this fact, he says that the responsible nervous factor in such instances does not exclusively involve the kidneys, but rather acts on the brain and resultant cerebral ischemic hypertension occurs. In such cases he adds, subarachnoid adhesion occurs with high frequency at the level of the upper thoracic segment.

In 1954, Maekawa³¹⁾ from Kyoto University studied 143 cases of neurocirculatory asthenia and reported that the cause of this disorder lay in the existence of subclinical arachnoiditis adhesiva cerebrospinalis. Individuals with this disorder revealed subarachnoid adhesion myelographically mainly at the level of cervico-thoracic cord segments C_1 — T_8 , a level corresponding to the site of the vasomotor centers innervating the lungs and heart. Because of this adhesion, there occurs an abnormal change in these autonomic nerves and disturbance of the spinal ganglia which, in turn, leads to the development of fatigability, palpitation, anxiety, breathlessness and similar sorts of symptoms which the subjects with neurocirculatory asthenia often show.

From such basis of evidence Maekawa inferred that subclinical arachnoid adhesion is a disease of frequent incidence which in itself never causes a serious damage to the organism but keeps stimu-

lating the sympathetic nerve, stimulus after a stimulus in summation whenever there is a stimulus from outside, to alter the sympathetic tone of the organism.

The author of this communication wanted to clarify whether or not an individual with subclinical arachnoiditis has his spinal sympathetic center a state of functional stimulation. For this purpose the author performed C. P. T. on 60 in-patients and animals, the following is a report on this investigation.

CHAPTER 3 METHOD OF EXPERIMENT AND MATERIAL

1) The C. P. T. has been performed on 56 in-patients, including 16 cases of essential hypertension, 27 cases of neurocirculatory asthenia, 8 cases of brain diseases, 9 cases of spinal cord disease and other one case. A C. P. T. was made after a patient had rested for 10 minutes in supine position. Since cold stimulus had to be applied to various parts of the body, it was impossible to adhere to the original method of Hines and Brown. Therefore, the author employed a method to place a ice piece, with cross section of 15 by 15 cm, each for one minute against the forehead, palms on the right and left, chest, abdomen, soles on the right and left of a patient examined. Blood pressure was made to transmit from the brachial artery, through a vinyl tube, to Hamilton manometer which sketched the pressure fluctuation on a oscillographic paper. C. P. T. was performed at various parts of the body each for 1 minute, and a 3 minute interval was made to intervene between each two tests. Respirator movement was also sketched whenever necessary.

2) apparatus

The apparatus to sketch blood pressure included: a dark box, 1.5 m long as shown in Fig. 2, an oscillograph-paper-roller (paper has the size of 8.8 cm × 25 m), source of light, 6 V, and a Hamilton manometer and an apparatus to drip the saline solution containing Heparine. These were joined together as is shown in Fig. 1, the apparatus was operated in the following way: the air in contact with a solution-reservoir in Fig. 1 was brought to about 180 mmHg in pressure with the aid of a rubber pumping-ball, and then, turning the three way stop-cock, the saline solution was allowed to jet out of the needle. Now this outflow of solution was stopped by turning a stop-cock attached to the dripping-tube and the needle was introduced into

the artery. As soon as arterial blood began flowing back through the needle, three way stop-cock at the dripping-tube was released to allow the outflow of the saline solution to wash out the blood. Dripping was continued for about 1 to 2 minutes. The needle was fixed tightly at the fore-arm of the patient examined. When washing out of the blood is completed, the three way stop-cock was turned so that the pressure at needle will be transmitted to Hamilton-manometer. The light was now put on and arterial blood pressure fluctuation was observed. Film began moving and blood pressure was sketched continuously. In the meantime an ice-piece was applied to the patients sole, abdomen, chest, palm and forehead, each for one minute.

Fig. 1 Schematic sketch of the apparatus employed in this experiment

Sphygmomanometer, Rubber pumping-ball, "Pressure-bottle" containing physiological saline solution, Dripping-tube, Three way stop-cock, Hamilton manometer, Catheter, Needle for venepuncture, Dark box, Source of light, 6 V, 8.3cm×25m oscillograph-paper roller.

Fig. 2 General view of the apparatus
From left: Film-roller, Dark box, Three way stop-cock, Catheter, Venepuncture needle.
Above: Quick-silver sphygmomanometer, "Pressure bottle", Pumping ball.

Everytime one test was over, the three way stop-cock was turned to wash out the saline solution, these preventing the obliteration of the needle with clot. A 3-minute interval was allowed to intervene between every two test. However, owing to the continuous sketching of blood pressure, it was easy to measure standard blood pressure with accuracy, a procedure necessary for determining the magnitude of a given pressor response. With this apparatus, it was also possible to depict minor elevation of blood pressure and tell whether it was respiratory in origin or a cold pressor effect.

Fig. 3 Hamilton-manometer

This Hamilton manometer is provided with an apparatus whereby to draw the standard line, which becomes the basis of the calculation of a blood pressure at given time.

Fig. 4 Specific curve of the author's Hamilton manometer for various values of blood pressure

A broad line at the center is the standard line. The series of shorter line in stair-case shape from a curve, which is the specific curve of this Hamilton manometer for various values of blood pressure. Which the aid of a quick-silver sphygmomanometer, the Hamilton manometer was made to grade the blood pressure for every 10mmHg of increase.

Fig. 5 C. P. T. at the forehead
The patient's right brachial artery is punctured by the needle connected with Hamilton manometer. This photograph shows how an ice ball, about 15 cm square in section, is applied to the patient's forehead for one minute.

Fig. 6 C. P. T. at the Left Palm
This photograph shows a patient under a C. P. T. with an ice ball applied tightly to his left palm for one minute, while the pressure of his right brachial artery is transmitted to an oscillograph paper.

Fig. 7 C. P. T. at the Right Palm
A C. P. T. with an ice ball applied to a patient's right palm.

CHAPTER 4 RESULTS

1) Cold pressor test in essential hypertension

The result of the C. P. T. in subjects with essential hypertension is tabulated in Table I. This table indicates that, generally, there is an increased cold pressor response at the palm, while cold pressor response is markedly reduced at the sole. The cold pressor response at the forehead simulates the cold pressor response at the palm in its magnitude in the majority of the cases, however, there is occasional inhibition exclusively of the cold pressor response at the forehead. (Fig. 11, 13, 14)

Of 17 subjects with essential hypertension, the following paragraphs give explanation to some of them showing typical response.

Fig. 1, 2, 3, 4 present four subjects in whom palm and forehead gave increased pressor response, but sole gave very weak pressor response. Fig. 5 presents a subject in whom palm gave strong pressor response, but forehead and sole gave weakened response. Fig. 6 shows a subject who has a greatly impaired pressor response from the abdomen and sole. Fig. 7 shows a C. P. T. in a subject following the intraarterial administration of Hexamethonium, 3.5%, in dose of 1cc. This figure shows the strong inhibitory effect of the intraarterial Hexamethonium on C. P. T.. Fig. 8 shows a C. P. T. in a subject with recovered essential hypertension. He gave still impaired pressor response at the abdomen, but nearly normal response elsewhere. Fig. 9 shows a pressor response which is different from the right palm to the left palm by as large as 40 mmHg. Fig. 10 gives a C. P. T. in a subject with essential hypertension complicated by the subarachnoid bleeding. He gave very impaired pressor response everywhere, and even a reverse response at the forehead. Fig. 11 presents a subject who gave extremely impaired pressor response only at the forehead. Fig. 12 indicates a C. P. T. in which the base line blood pressure became elevated while tests were repeated. The base line blood pressure failed to return to the previous level even 3 or 5 minutes after the cessation of the cold stimulus. Fig. 13 presents the C. P. T. in a subject who, like the other subject of Fig. 11, had an extremely impaired pressor response only at the forehead. Fig. 14 shows a C. P. T. exclusively impaired at the forehead, chest and left sole.

1) The photographs, from the top to the bottom, are in the order of the performance of the test. Interval

TABLE I C. P. T. IN HYPERTENSIVE SUBJECTS

Sex	Age	Diagnosis	B. S. L. mmHg	Systolic Response mmHg							Myelography
				R. Palm	L. Palm	Forehead	R. Sole	L. Sole	Abdomen	Chest	
♂	50	E. H. T.	170-70	45	50	50	0	0	10	40	—
♀	63	E. H. T.	150-60	60	60	50	20	20	10	30	—
♂	55	E. H. T.	150-30	40	40	40	0	0	0	—	—
♂	66	E. H. T.	220-80	40	60	20	0	0	—	—	—
♂	53	E. H. T.	150-40	60	60	40	10	5	20	20	—
♀	72	E. H. T.	160-40	30	30	20	15	15	20	—	—
♂	52	E. H. T.	200-110	60	40	80	30	30	—	—	T_8-L_2
♀	35	E. H. T.	170-90	20	20	20	0	0	—	—	C_6-7, T_{1-11}
♂	60	E. H. T.	150-80	80	40	15	20	20	—	—	T_{4-8}
♀	42	E. H. T.	260-130	50	50	30	25	25	—	—	T_2-L_1
♂	19	R. H. T.	150-50	30	25	0	20	0	20	—	—
♂	31	R. H. T.	160-90	50	60	0	40	40	40	—	C_2-6, T_9-L_1
♂	55	E. H. T.	160-90	30	70	20	0	5	—	—	C_2-6, T_{8-12}
♂	25	E. H. T.	170-70	60	70	30	50	50	—	—	—
♀	54	E. H. T.	160-90	10	10	-10	-10	0	—	—	—
♂	35	Recovered	110-60	20	20	20	20	20	15	—	—
♂	45	E. H. T.	185-80	15	10	15	15	15	—	—	C_2-5, T_{8-10}

E. H. T. Essential Hypertension

R. H. T. Renal Hypertension

B. S. L. Base Line Blood Pressure (Systolic and Diastolic blood pressure in mmHg unit)

Systolic Response: Systolic Blood Pressure Response induced by the application of stimulus to the palm, sole, forehead etc.

Myelography; Location of the subarachnoid adhesion as revealed by the myelography.

Fig. 1. Male, 53 Years Old, E. H. T.

This patient responded very poorly to a cold stimulus applied to his sole. However, he showed as sharp response as 60 mmHg pressor effect when his palm was stimulated. Pressor effect from his left sole and right is greatly different, one from the right sole being larger by 20 mmHg or more.

of each 3 to 5 minutes was allowed to intervene between any two tests.

2) One or two straight horizontal lines indicate the standard line of the blood pressure.

3) The oscillating waves indicate the arterial

Fig. 2. Male, 55 Years Old, E. H. T.

Pressor effect from his abdomen and soles was poor, while pressor effect from the palms and forehead was as large as 40 mmHg or more.

pressure. Increase in the arterial pressure is shown by the upward shift of the oscillating waves.

4) A small, vertical line and another vertical line at a certain distance indicate the beginning and the end, respectively, of the application of cold stimulus.

5) Tapering, fine, vertical oscillation is due to the timer.

6) Fig. 9, 10 and some others contain a grossly fluctuating curve. This is the curve of the respiratory movement.

7) Some figures (Fig. 12, 13 etc) contain double waves of the arterial pressure. One stands for the right, the other stands for the left brachial artery,

synchronously.

8) Magnitude of the observed pressor effect is indicated numerically each time in the space above the film. Such notification as "R. Palm", "Forehead", etc. specifies the site chosen for the stimulus application. "B. L." means the base line blood pressure prior to the C. P. T.; "Ce." means the maximum rise in the blood pressure, or ceiling; "Re" means the magnitude of the cold pressor effect.

Fig. 3 63 Years Old, E. H. T.
Pressor effect from the sole and abdomen was poor. Pressor effect from the forehead and palms was larger than 60mmHg.

Fig. 4 Male, 50 Years Old, E. H. T.
Pressor effect from the soles was poor. Stimuli to his forehead, palms and chest elicited marked pressor response, each exceeding 40mm Hg.

Fig. 5 Male, 66 Years Old, E. H. T.
Pressor effect from the sole, forehead was poor. His palms gave marked pressor response, larger than 40 mmHg.

Fig. 6 Female, 72 Years Old, E. H. T.
She gave a poor pressor response to a stimulus on the abdomen. Pressor effect from the palms was 30 mmHg.

Fig. 7 Female, 42 Years Old, E. H. T.
Pressor effect from her soles was poor. Administering Hexamethonium 3.5% in dose of 1cc intraarterially exerted a pronounced inhibition effect on the cold pressor response. Her Myelography revealed the subarachnoid adhesion at the level of D 3, 5, 8, 10, 12 and L 1 spinal cord segment.

Fig. 8 Male, 35 Years Old, Recovered E. H. T.

Except for a slightly reduced pressor response from abdomen, he gave moderate pressor response everywhere. The administration of T. E. A. C. blocked the pressor response. His myelogram revealed as subarachnoid adhesion at the level of D 5-10.

Fig. 9 Male, 55 Years Old, E. H. T.

He is particular in that his left and right palm gives as discrepant pressor response as by 40 mm Hg. His myelogram revealed a subarachnoid adhesion at the level of C 3-7. Pressor effect from his soles was in the order of 20 mmHg., and was much poorer than that from the palms. His cold pressor curves were recorded simultaneously with a respiration curve.

Fig. 10 Female, 54 Years Old, E. H. T. with Paroxysms, Encephalopathy, Meningovascular Syphilis.

She is particular in that her forehead gives an inverse response -10 mmHg. She also gives discrepant pressor response from the right palm to the left, difference being about 20 mmHg. Her condition is hypertension, but her pressor response is nowhere hyper-reacter typed.

Fig. 11. Male, 25 Years Old, E. H. T.

Pressor effect from his sole was as great as that from the palms, both exceeding 50mmHg; however, pressor effect was almost nil from the forehead. Respiration curve was recorded synchronously with the pressor curve.

Fig. 12. Male, 60 Years Old, E. H. T.

This pressor curve is particular in that his blood pressure, elevated by the first C. P. T., had not completely returned to the previous level by the time of the second C. P. T. With the result that the base line blood pressure for the 2nd C. P. T. was higher, and the pressor response magnitude therefore relatively smaller. In the other words, the second C. P. T. gave a high ceiling but small response.

Fig. 13. Male, 31 Years Old, R. H. T.

Pressor effect from the soles and palms were over 40mmHg. In contrast, forehead gave no pressor response whatever. His myelogram revealed a subarachnoid adhesion at the level of C 2-7 and D 9-11.

Fig. 14 Male, 19 Years Old, R. H. T.
Pressor effect was poor from his forehead, chest and left sole. Pressor effect was normal elsewhere.

2) THE COLD PRESSOR TEST IN NEUROCIRCULATORY ASTHENIA

The cold pressor test was performed each on 27 cases of the neurocirculatory asthenia. The results are listed in Table II. Average magnitude of the pressor effect was; from palms, 22 mmHg: from forehead, 15 mmHg: from soles 8 mmHg.

Patients with neurocirculatory asthenia are particular in that their pressor response to cold is usually as small as 10 mmHg or less, whatever part of the body may be stimulated. However, average pressor effect from the palms appears exceptionally great. (its average value being 22 mmHg.) This is due to the fact that a small number of the patients without cervical arachnoiditis showed very pronounced pressor effect from their palms. (Table II) On the other hand, the pressor effect from the soles is unanimously poor. On average it is as small as 8 mmHg or less. Pressor effect from the forehead is 15 mmHg on an average. It appears well to conclude that the patients with neurocirculatory asthenia gave very poor cold pressor response throughout the body.

Fig. 15 to Fig. 18 present four subjects with complete loss of the pressor response throughout the body. Fig. 19 shows a subjects with poor pressor effect from the forehead and left sole. Fig. 20 illustrates a contrast between moderate pressor effect from the palms and very poor pressor effect from the soles in patient with thraco-lumbar arachnoiditis. Fig. 21 presents a subjects who gave an extremely great pressor response to a stimulus on the forehead. (Administering Apresolin in does of 20mg. did not significantly alter the pressor response.) Fig. 22 shows very poor pressor effect from the abdomen. Fig. 23 shows an extremely great pressor effect from the palms.

TABLE II C. P. T. IN NEUROCIRCULATORY ASTHENIA

Sex	Age	Arachnoiditis		Response mmHg					
		Myelography	B. S. L. mmHg	L. Palm	R. Palm	Forehead	L. Sole	R. Sole	Abdomen
♀	46	C ₇ , T ₁₋₁₂ , L ₁	150-70	10	20	—	0	0	—
♂	20	C ₅₋₇ , T ₇₋₁₂	90-50	10	0	10	0	0	—
♂	27	C ₄₋₆ , T ₃₋₁₂	105-50	15	15	25	0	0	—
♀	34	C ₄₋₆ , T ₃₋₆ , L ₁₋₃	150-70	15	15	20	0	0	—
♀	30	C ₃₋₇ , T ₃₋₇ , L ₁₋₃	100-50	0	0	-10	10	5	—
♀	31	C ₃₋₇ , T ₅₋₁₂ , L ₁₋₃	90-40	20	20	5	10	5	—
♂	27	T _{7-L3}	100-40	20	20	20	15	15	—
♂	22	—	100-40	20	20	20	10	10	—
♀	30	C _{7-T8} , L ₁₋₂	120-50	0	5	20	5	5	20
♂	23	C ₃₋₆ , T ₃₋₁₂	145-70	15	15	0	0	0	—
♀	38	C ₃₋₅ , T ₁₋₁₂ , L ₁₋₂	120-50	10	10	20	10	10	—
♂	18	—	90-20	—	20	10	0	—	—
♀	33	—	100-30	—	0	5	5	—	—

♂ 45	—	110-50	—	10	0	10	—	—
♀ 22	C ₆₋₇ T ₁₋₁₂	100-35	10	10	10	20	10	0
♀ 33	—	100-40	0	0	0	0	0	—
♂ 48	T _{1-L} ₃	110-60	20	20	60	10	0	20
♀ 30	T _{2-L} ₃	90-30	30	30	30	0	0	—
♂ 39	T _{2-L} ₁	80-25	70	60	40	20	20	20
♂ 29	T ₂₋₉	90-30	50	50	30	20	20	0
♂ 18	T _{2-L} ₁	90-50	40	40	55	0	20	—
♂ 55	T ₈₋₁₂	120-50	50	45	5	10	10	—
♂ 50	T _{7-L} ₁	80-50	60	60	—	20	20	—
♂ 24	T _{9-L} ₂	90-40	40	30	20	5	0	—
♀ 40	T _{7-L} ₁	130-80	30	30	10	10	0	—
♂ 24	C ₇ , T _{1-L} ₂	85-30	10	10	10	5	10	—
♂ 46	T _{7-L} ₅	90-35	30	30	40	10	0	—

Myelography: Location of the subarachnoid adhesion as revealed by myelogram. (C. cervical, T. thoracic, L. lumbar)

B. S. L.: Base Line Blood Pressure (systolic and diastolic blood pressure in mmHg).

Response: Cold pressor effect from the palms, forehead, soles and elsewhere, each in mmHg.

Fig. 15 45 years old, N. C. A.

He gave very poor pressor response everywhere, excepting for his left palm which responded normally with 20 mmHg of blood pressure elevation.

Fig. 16 36 years old, N. C. A.

In this instance blood pressure from both brachial arteries and respiration were recorded synchronously.

Pressor response was poor everywhere, particularly at the palms and forehead.

His myelogram revealed subarachnoid adhesion at the level of C. 7, D. 1-10, L. 1.

Fig. 17 34 Years Old, N. C. A.

Pressor response was poor everywhere, particularly at the soles.

Fig. 18 38 Years Old, N. C. A.

This patient is particular in that his palms give especially poor pressor response, while his forehead, soles give normal response.

His myelogram is that of the subarachnoid adhesion at the level of C. 5, D 1-3, 6-9.

Fig. 19 40 Years Old, N. C. A.

Her respiration curve was recorded synchronously with the cold pressor curve. Pressor effect is particularly poor from the forehead and sole.

Her myelogram is that of the subarachnoid adhesion at the level of D. 7-L. 1.

Fig. 20 24 Years Old, N. C. A.

Respiration was recorded synchronously. Pressor effect from the sole is very poor and makes a contrast to that from the palms.

Myelographically, subarachnoid adhesion is suspected at the level of T. 9-12 and L. 1-2.

Fig. 21 48 Years Old, N. C. A.

His forehead gave an extremely large pressor response. In contrast, his body below neck characteristically gave small pressor response, 20 mmHg or less. Administering Apresolin in dose of 20mg intraarterially did not block the pressor response.

His myelogram is that of the subarachnoid adhesion at the level of D. 1-12 and L. 3.

Fig. 23 39 Years Old, N. C. A.

Pressor effect from the palms is extremely marked, reaching 70mmHg. In contrast, pressor effect was poor from the chest and left sole.

His myelogram was that of the subarachnoid adhesion at the level of D. 2-12 and L. 1.

Fig. 22 29 Years Old, N.C. A., Ulcer Duodeni

Pressor responses from his abdomen and soles were very poor in contrast to a good response from the palms.

His myelogram was that of subarachnoid adhesion at the level of D. 2-11.

3) C. P. T. AND SPINAL CORD INJURY

The C. P. T. was performed on each of 8 cases. The results are listed in Table III. Pressor effect from the involved localities were markedly weakened by the presence of spinal cord injuries.

Fig. 24 to 26 present 3 patients with subarachnoid hemorrhage and myelitis with accompanying motor and sensory disturbance of the limbs and trunk. Area of inhibited cold pressor response coincided with the area of the sensory disturbance. Fig. 27 presents a patient after the resection of the right posterior root of the 5th lumbar and 1st, 2nd sacral segment. Pressor effect from the right sole was completely blocked.

Elsewhere, area of the complete block to pressor response coincided with the locality of strong hemorrhage, namely, the chest and abdomen. Fig. 28 presents a patient with lateral sclerosis associated with the motor disturbance of the upper and lower extremities. He gave very pronounced pressor

TABLE III C. P. T. AND SPINAL CORD INJURY

Diagnosis	Spinal lesion			Response mmHg								
	Age	Sex	Myelography	B. S. L. mmHg	L. Palm	R. Palm	Fore head	L. Sole	R. Sole	Abd- men	Chest	Thigh
Myelitis	♀	54	D ₅ -L ₄	80-20	40	40	40	10	10	20		
Tetraplegia	♀	35	C ₁₋₄ , D ₅₋₁₀	100-30	10	10	20	0	10	0	—	20
Myelitis	♀	36	D ₅ , D ₈₋₁₀	90-45	20	20	20	10	10	10	—	—
Hereditary Ataxia	♀	43	D ₄₋₁₂ , L ₁₋₅	120-40	40	40	50	20	15	—	—	—
Hematomyelia	♂	28	C ₄ -D ₁₂	100-50	20	0	20	20	0	0	0	10
Hematomyelia	♀	30	D ₄ -D ₁₂	150-60	25	10	15	10	15	0	0	—
Poliomyelitis	♂	22		110-50	20	30	10	10	20	—	—	—
Amyotrophic lateral sclerosis	♂	43	C ₆₋₇ , D ₂₋₄	120-60	20	20	40	20	20	—	—	—

Myelography
B. S. L.
Response } same as Table II.

response at the forehead. (Poor pressor response from the left sole may be due to the presence of

subarachnoiditis) Fig. 29 shows a patient with hereditary ataxia with accompanying sensory disturbance of the lower extremities. Pressor effect from the soles was nil. He also gave a strong response to a stimulus at the forehead. Fig. 30

Fig. 24 35 Years Old, Subarachnoid Hemorrhage, Tetraplegia

This is an instance of subarachnoid hemorrhage with tetraplegia. Excepting the normal response (20 mmHg) at forehead and left thigh, pressor response was inhibited elsewhere.

His myelogram was that of the subarachnoid adhesion at the level of C. 1-4 and D. 4-12.

Fig. 25 34 Years Old, Sensory Motor Disturbance of Extremity.

This is an instance of subarachnoid hemorrhage with sensory and motor disturbance of four extremities. Pressor effect was minimal at the chest, abdomen and soles.

His myelogram revealed a subarachnoid adhesion at the level of D. 5-11.

shows a C. P. T. which was performed during a seizure of narcolepsy. Pressor effect was nowhere inhibited. Fig. 31 presents a diabetic accompanied by right-sided hemiplegia. Pressor response, how-

ever, did not differ from the right to left. This patient gave poor pressor response throughout the body. Fig. 32 presents a C. P. T. on a patient with intermittent claudication at one of the intervals between attacks. No marked change was noted.

Fig. 26 54 Years Old, Myelitis

Pressor effect was poor from the forehead, soles and abdomen. Pressor effect from abdomen differed from the right to left, left half giving strong response than the right by 10 mmHg. On the left half of the abdomen application of the cold stimulus elicited a transient elevation of blood pressure from the moment the stimulus reached the skin, owing to an impulse from the superficial cold sense ending. This transient elevation of blood pressure was in the order of 20 mmHg and without a latent period preceding the pressor response.

Her myelogram revealed subarachnoid adhesion at the level of D. 5-11 and L. 1-4.

Fig. 27 28 Years Old, Hematomyelia

In this patient with spinal hemorrhage at the level of the cervical segment, there was an overall sensory and motor disturbance excepting left arm. He had been operated upon for resecting the right posterior roots entering the 5th lumbar, 1st and 2nd sacral segments, and was without sense at the right sole.

A C. P. T. on this patient revealed a complete block to the pressor response at the right sole, corresponding to the region of the previously resected posterior roots, and at the right palm, chest and abdomen, corresponding to the injured portion of the spinal cord.

His myelogram revealed subarachnoid adhesion at the level of C. 4-7 and D. 1-12.

Fig. 28 43 Years Old, Amyotrophic Lateral Sclerosis
Pressor effect was as large as 40mmHg at the forehead, but as poor as 20mmHg at the palms and soles.

This patient had a pronounced motor disturbance in the legs in the complete absence of sensory disorder.

Myelographically, subarachnoid adhesion was suspected at the level of C. 6-7. D. 2-4.

Fig. 29. 43 Years Old, Hereditary Ataxia
Pressor effect was great from the palms and forehead, but very poor from the soles.
This patient is now unable to walk. She has a sensory disturbance.

Fig. 30 30 Years Old, Narcolepsy, Grandmal, Epilepsy
The C. P. T. in this patient was performed during a seizure of Narcolepsy, but no inhibition to the pressor response occurred. Pressor effect was over 20mmHg throughout the body.

Fig. 31 48 Years Old, Diabetes Mellitus, Hemiplegia
 This patient was a diabetic with right-sided hemiplegia. Pressor effect was not different on the right and left. Pressor effect was generally very weak.

4) BLOOD SUGAR AND C. P. T.

Blood sugar level was studied before and after C. P. T. in four cases. The results are listed in Table IV. It was noted that institution of a C. P. T. at a locality caused the blood sugar level to rise by about 4 mg/dl, with further rise in the blood sugar level each time another C. P. T. is instituted, so that the final blood sugar level after 5 C. P. T. was higher than the original level on average by 10 mg/dl. One of the 4 cases studied showed steady increase in the base line systolic pressure along with increase in blood sugar level each time C. P. T. is repeated, while rest of them did not show any change in base line pressure. Increase in blood sugar level could not be correlated with the magnitude of the pressor effect.

Fig. 32 42 Years Old, Arteriosclerosis of the Extremity
 This patient had intermittent claudication in left leg, and a C. P. T. was made in one of the intervals between attacks. This C. P. T. revealed slight weakening of the pressor effect from the left sole.
 His myelogram was that of subarachnoid adhesion at the level of D. 8-12.

TABLE IV C. P. T. AND BLOOD SUGAR

Sex	Age	Order	The Locale applied Cold Stimulus	Blood Sugar mg/dl	B. S. L.	Response	Diagnosis
♀ I	30	0	—	80	140/50	mmHg	Hematomyelia
		I	Forehead	—	140/50	160/70/20	
		II	R. Palm	84	145/55	160/70/15	
		III	R. Sole	—	150/65	165/70/15	
		IV	L. Sole	—	150/65	165/70/15	
		V	L. Palm	90	155/70	165/70/10	
♂ II	46	0	—	85	90/35	mmHg	Asthma bronchiale
		I	Forehead	—	90/35	125/50/35	
		II	R. Palm	—	90/35	125/50/35	
		III	R. Sole	90	90/35	100/50/10	
		IV	L. Sole	—	90/35	130/50/40	
		V	L. Palm	95	90/35	125/50/35	

♀	34	0	—	71	90/45	mmHg	Neuro circulatory Asthenia
		I	Forehead	73	90/45	110/50	
		II	R. Palm	—	90/45	110/50	
		III	R. Sole	—	90/40	100/45	
		IV	L. Sole	—	90/45	105/48	
		V	L. Palm	83	90/45	110/50	
♂	66	0	—	76	210/70	mmHg	Essential Hypertension
		I	Forehead	80	210/70	230/80	
		II	R. Palm	—	210/70	270/110	
		III	R. Sole	—	220/80	220/80	
		IV	L. Sole	—	210/70	210/70	
		V	L. Palm	85	220/80	260/100	

5) THE ADMINISTRATION OF ADRENALIN AND C. P. T.

C. P. T. were performed in 4 cases after the administration of Adrenalin subcutaneously, but

rest of them through the arterial route.

Following the subcutaneous administration of Adrenalin in does of 0.4cc, the basal blood pressure level became elevated, but cold pressor effect was reduced somewhat. (Fig. 33)

Following the intraarterial administration of Adrenalin in does of 0.1cc, there occurred tachycardia and increase in pulse pressure, (Fig. 34), but no change in cold pressor response.

Following the intraarterial administration of Adrenalin in dose of 0.05 cc, pressor effect from sole was much weakened two minutes after the administration. (Fig. 35)

With 0.01cc of intraarterial Adrenalin, Cold pressor response was completely blocked and inverse response — 10 mmHg occurred 2 and 4 minutes after

Fig. 33 Pseudobulbar Palsy

Pressor effect in this patient was: from palm, 60 mmHg, from forehead and abdomen, 30 mmHg, from soles, 10 mmHg, thus showing marked variation in the pressor effect from place to place of the body, which is provably due to a coexisting arachnoiditis.

In this patient the effect of Adrenalin in dose of 0.4cc subcutaneously on C. P. T. was studied. At the end of ten minutes when basal blood pressure level reached the peak, cold pressor effect did not increase but decrease.

Fig. 34 30 Years Old, Asthma Bronchiale

Effect of the intraarterial Adrenalin in dose of 0.1cc on C. P. T. was studied. Following the administration of Adrenalin, there occurred increase in pulse pressure, but no change in cold pressor response.

the administration. (Fig. 36)

Fig. 35 46 years Old, Asthma Bronchiale
A C.P.T. was made after administering 0.05cc of Adrenalin through the arterial route. Cold pressor response was markedly depressed.

[Fig. 36 Asthma Bronchiale
A C.P.T. was performed following the intra-arterial administration of Adrenalin in dose of 0.01cc. In this case cold pressor effect was reversed into a cold depressor response, -15mmHg at the soles and palms.

DISCUSSION

Above experiments disclose that the cold pressor response in one and the same subject is not uniform throughout the body, but different from part to part. As was mentioned in the introduction to this paper, this fact is due to the lack of uni-

Fig. 37 C. P. T. at the Sole and Abdomen in Dog.
(Effect of a large dose of Adrenalin on C. P. T.)

I) Intravenous drip infusion of Adrenalin in dose of 0.2cc in dog caused the blood pressure to rise as much as 100mmHg or more within 10 seconds and fall, upon cessation of the drip infusion, in straight line fashion over the period of about 3 minutes.

II) 5 minutes after such fall in blood pressure had occurred, blood pressure was again measured. The result was that the basal blood pressure level was found lower than before the administration of Adrenalin by more than 20mmHg. Interesting enough, the dog in such condition failed to respond to the application of dry-ice.

III) Similarly, at the end of 10 minutes no pressor response could be elicited.

Note: Temperature of the local tissue was also recorded. It is presented as a descending straight line in each of the graph papers.

Fig. 38 Effect of a large dose of Adrenalin on C.P.T.
(Dry-ice was used. C.P.T. at the soles in dog)
I) A C.P.T. before the administration of Adrenalin showed elevation in blood pressure by 30mmHg.

II) Adrenalin was administered drip wise intravenously in dose 0.3cc. Following a transient fall, there occurred an immediate rise in blood pressure, reaching 130mmHg. After blood pressure had returned to the previous level, a C.P.T. was performed. Cold pressor response was found extremely weakened, owing to the premedication with Adrenalin.

Fig. 39 The length of time necessary for the elevated blood pressure to return to the previous level, and its relation to the temperature of the local tissue.

I) A C. P. T., applying dry-ice to the dog's abdomen for one minutes caused the blood pressure to rise and the local tissue temperature to fall at the same time. Upon removal of the stimulus after one minute, local tissue temperature kept descending and became lower than before C. P. T. by 12°C . 2 minutes after removal of the cold stimulus, local temperature began to ascend slowly and soaring blood pressure began to descend, simultaneously. At the end of 3 minutes local tissue temperature rised somewhat and blood pressure returned to the previous level.

II) A C. P. T., employing ice-ball, was performed at the abdomen in dog. After 1 minute local temperature fell by 6°C , but, at the end of 2 minutes, both local temperature and blood pressure returned to the previous levels.

Fig. 40 Magnitude of cold pressor effect, and its relation to the length of time necessary for the blood pressure to return to the pre- C. P. T. level.

Relation between the magnitude of pressor response and the length of time necessary for the blood pressure to return to the previous level. It applies to every case that recovery of blood pressure is effected in about 30 seconds.

This arrangement of photographs is in descending order of the pressor effect magnitude. As to the instance of as large pressor response as 50 or 60 mmHg, it took blood pressure only 15 to 23 seconds to return to the previous level. By contrast, as to the instance of as small pressor response as 30 mmHg, it took blood pressure as long as 45 seconds to descend to the previous level. It means that there is no linear relation between the magnitude of pressor response and the length of time necessary for the blood pressure to return to the previous level.

formity in excitability among spinal sympathetic nerve centers at different spinal cord levels. Such luck of uniformity in excitability can be explained by the presence of spinal subarachnoid adhesion. Actually, Konishi from this laboratory noticed the incidence with high frequency of subarachnoid adhesions myelographically at the level of the lower thoracic and upper lumbar segments, where lies the sympathetic nerve center for the sole and abdomen, in the patients with essential hypertension. Patients with E. H. T. gave weakened cold pressor response at their soles and abdomen.

Myelogram in the patients with neurocirculatory asthenia are often that of diffuse subarachnoid adhesion extending from the cervical to lumbar segments, and this fact explains the results of C. P. T. in such subjects.

Pressor response in such subjects are weakened everywhere. These fact constitute evidence that there existe a close relation between subarachnoid adhesion and weakened cold pressor response.

It follows, therefore, that the problem of hyper-reactor or hyporeactor may be related not only to the question of disposition (sympaticotonia or vagotonia), but to the presence or absence of spinal cord disturbances. For example, one person may exhibit a cold pressor response of hyporeactor-type at his palm, but that of hyperreactor-type at his forehead, and this was the case with many subjects studied by the author. (Fig. 21)

Such difference in C. P. R. also occurred between two palms. (Fig. 9) Such is the example of localized impairment of cold pressor response, and this may be caused in two ways:

1) With intact cold pain of uniform intensity everywhere in the body, there may be conduction disturbance somewhere in the afferent path way of such cold pain.

2) There may be localized disturbance of the cold pain sense itself.

(It is an interesting fact that certain parts of the body, ear auricle and glans penis for example, are normally irresponsive to a cold stimulus.)

In connection with the first possibility, or impaired afferent conduction of the cold pain, Fig. 27 is of interest. Namely, in this instance resection of the right posterior roots abolished the cold pressor response from the right sole.

It was postulated in the introduction that an afferent impulse, arising in the blood vascular wall,

reaches the spinal cord via posterior roots, and ascends through Tr. spinothalamicus to reach the thalamus. If this is the case, such condition as affecting afferent conduction of an impulse, subarachnoid hemorrhage, hereditary ataxia, for instance, may inhibit the transmission of cold pain impulse to the center, hence impaired pressor response.

In fact, pressor response from the soles is impaired most frequently, and this appears due to disturbance of the afferent pathway in the spinal cord. The reason is this: the afferent pathway in the spinal cord is the most peripheral seated and the longest for an impulse from the sole in comparison with impulse from elsewhere, and so an impulse from the sole is most prone to be involved in existing subarachnoid adhesion.

Here rises a question: why is the pressor response from the forehead impaired so often and exclusively?

There is another point suggesting that an impaired pressor response is not caused by afferent conduction disturbance. It is the fact that the subjects with arachnoiditis have intact sense everywhere or even increased sensitivity in many cases. In view of this fact, the inference that an impaired pressor response is due to the disturbed conduction of an afferent impulse sounds not likely, because such inference is based on the assumption that impairment occurs only on the afferent pathway of the cold pain, and not on that of other senses.

Therefore, the explanation for an impaired pressor response should be sought in the 2nd possibility, namely, localized failure of the body to give out sufficient cold pain.

It should be noted that the intensity of a cold pain is dependent on the condition of the local blood vessel subjected to a cold stimulus, namely, a blood vessel which is originally in the state of moderate constriction does not give out much cold pain upon the application of a cold stimulus, while a blood vessel in the state of dilatation give out strong cold pain when subjected to a cold stimulus.

Such tone of the blood vessel depends upon the innervation from the spinal sympathetic nerve center, so any condition tending to the excitement of a spinal sympathetic center bring the blood vessels in the corresponding area in the state of vasoconstriction and makes them less responsive to a cold stimulus. One example of such excited condition of the spinal sympathetic center is, as

was mentioned earlier in the chapter of the purpose, the one caused by a subarachnoid adhesion. In the presence of an adhesion, no matter how small it is, spinal sympathetic center is exposed to continuous stimulation and is lead to a state of lasting excitation.

With regard to the relation between an excited spinal sympathetic center and intensity of artificially evoked cold pain, the following data are available.

1) As is shown in Fig. 33—36, 37, the administration of Adrenalin, subcutaneous or intravascular, leads to a very impaired cold pressor response.

2) With a C. P. T. at the soles or palms there occurs vasoconstriction in the kidneys as well as in the splanchnic region. Some subjects with essential hypertension, in whom there exists already vasoconstriction in the kidneys, do not exhibit so great renal vasoconstriction during a C. P. T. as the normal subjects do. Subjects with essential hypertension with marked renal vasoconstriction at rest do not respond to a C. P. T. by a further renal vasoconstriction but by a vasodilatation, to the contrary. (Matsushita, Nara)

3) Manic-depressive patients and schizophrenic patients, who are off balance with regard to the neurovegetative tone, exhibit extremely weak or often reversed cold pressor response. (Igersheimer, 1953)

With lowered excitability of the sympathetic nerve:

1) As was mentioned in the introduction to this paper, Cannon, Wolf and Hardy demonstrated an enhanced response of the blood vessel, hence a marked pressor response from the area deprived of sympathetic innervation by removing perivascular distribution of the sympathetic nerve or by severing the sympathetic ganglia.

2) With blocked autonomic nerve by T. E. A. C., a C. P. T. produces cold pain of greater intensity than without T. E. A. C.. With T. E. A. C., efferent impulse to the splanchnic blood vessels is affected; however, owing to a strong cold pain in this condition, Epinephrine is discharged vigorously and this leads to a sustained pressor effect, sometimes. (Reiser and Ferris) This is an instance of the autonomic nerve blocking which leads to an enhanced cold pain. In the next place, some consideration must be made on the problem of the impaired efferent pathway of the cold pressor re-

flex.

The efferent pathway of the cold pressor response is that which descends from the thalamus and terminates at various levels of the spinal vasomotor center. Next fibers arise here and, passing through the sympathetic ganglia, terminate at the blood vessels of various regions. Among them, of the primary importance for a cold pressor response is the major splanchnic nerve. However, it is evidently impossible for an ordinary spinal lesion to be grave and bilaterally extensive enough to effect a blocking of this nerve. With such grave spinal injury, a man should exhibit a lowered blood pressure. Therefore, an impaired cold pressor response can not be explained in term of an injured efferent pathway. Similarly, the phenomenon of localized impairment of the cold pressor response can not be explained in this way.

To summarize, a cold pressor response may be impaired in two ways. Firstly, it may be impaired when there exists blocking to the afferent conduction of an impulse through the spinal cord; subarachnoid hemorrhage associated with sensory disturbance or hereditary ataxia, for example. Secondly, it may be impaired when a subject gives out only weak cold pain; subarachnoid adhesion not associated with sensory disturbance, for example.

It was shown in the preceding paragraph that the magnitude of a cold pressor response depends on the tone of the spinal sympathetic centers. With C. P. T., the author examined some number of the in-patients with essential hypertension and neurocirculatory asthenia. The results, as mentioned in preceding chapters, were that the subjects with essential hypertension exhibited impaired pressor response from their abdomen and soles, thus suggesting enhanced tone of the spinal sympathetic center at the level of the lower thoracic and upper lumbar segments.

In neurocirculatory asthenia pressor response was poor everywhere in the majority of the cases, thus suggesting enhanced tone of the entire spinal sympathetic centers.

On the other hand, many of the subjects with essential hypertension and neurocirculatory asthenia showed local variation in the cold pressor effect, and this fact seems due to different degree of subarachnoid adhesion from part to part along the spinal cord in them.

SUMMARY

I) With intact spinal cord, a cold stimulus evokes a pressor response of equal magnitude, wherever on the body surface may be stimulated. With subclinical subarachnoid adhesion, an apparently normal looking person gives out impaired cold pressor response at area corresponding to segments of the spinal cord involved in the adhesion. For example, with subarachnoid adhesion at the level of the lower thoracic and upper lumbar segments, a man gives impaired C. P. T. at his soles.

II) The author searched the reason why areas involved in subarachnoid adhesion should give out impaired cold pressor response. It was ascertained that it was because such adhesion brings the local spinal sympathetic center to a state of excitement.

III) With above facts in mind, the author performed C. P. T. on 56 in-patients admitted to this hospital. The results were as follows:

- a) The majority of the subjects with neurocirculatory asthenia gave poor pressor response everywhere, suggesting enhanced tone of the sympathetic center at every level of their spinal cords.
- b) In essential hypertension pressor response was poor from the abdomen and soles, suggesting excitement of the spinal sympathetic center at the level of the lower thoracic and upper lumbar segments.

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