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ARNOLD KATZ
M.B. Ch.B.

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On

RAYNAUD'S PHENOMENA

of the

UPPER EXTREMITIES

with special reference to

SYMPATHECTOMY

and

REGENERATION of the SYMPATHETIC

CONTENTS.

		Page.
I.	INTRODUCTION	1.
II.	THE SYMPATHETIC NERVOUS SYSTEM:	
	(a) History	3.
	(b) Anatomy and Physiology	
	1. Embryology	8.
	2. Central Representation	11.
	i. Cortex	11.
	ii. Hypothalamus	12.
	iii. Medulla	14.
	iv. Spinal Cord	14.
	3. Sympathetic Outflow to the Upper Extremity	
	i. Preganglionic	17.
	ii. Postganglionic	26.
	(c) Sympathectomy - A Review	30.
III.	RAYNAUD'S PHENOMENA:	
	(a) An Historical Review	39.
	(b) Etiology	43.
	(c) Symptomatology	49.
	(d) Pathology	53.
	(e) Diagnosis	61.
	(f) Treatment	61.
	(g) The Effect of Sympathectomy	62.
IV.	INVESTIGATIONS OF SYMPATHECTOMISED EXTREMITIES:	
	(a) Methods and Results	68.
	1. Sweating Test	68.
	2. Skin Resistance Test	112.
	3. Response to Pilocarpine	148.
	4. Plethysmography	204.
	(b) Summary and Conclusions	231.
	(c) Case Histories	233.

Page.

V. EXPERIMENTAL INVESTIGATIONS: 323.

(a) Anatomy and Physiology ..... 323.

(b) Operative Procedure and Post-operative Course ..... 349.

(c) Histology ..... 385.

VI. DISCUSSION ..... 411.

VII. SUMMARY ..... 426.

VIII. CONCLUSIONS ..... 428.

IX. RECOMMENDATIONS FOR FURTHER STUDY ..... 432.

X. ACKNOWLEDGMENTS ..... 434.

XI. BIBLIOGRAPHY ..... 436.

I. INTRODUCTION.

Almost 100 percent. of Raynaud's Phenomena of the lower extremities respond to surgical treatment. The treatment of Raynaud's Phenomena of the upper extremities, on the other hand, has occupied the attention of medical observers for over fifty years with little success. Surgeons, physicians, research workers, physicists and their associates have attempted to solve the problem and produce a rational solution.

It is well recognised that Raynaud, in his original thesis, described many conditions which are now no longer included under the syndrome which came to bear his name. Raynaud's "Disease" does not represent a disease entity. It is a symptom complex and, as such, numerous conditions may be responsible for the clinical manifestations which have been included in the group of conditions termed Raynaud's "Disease".

As Lewis and Pickering (1934) realised, Raynaud's "Disease" could not be regarded as the result of one set of circumstances. They suggested, therefore, that the term should be abandoned and instead the words Raynaud's "Phenomena" be used.

Thus the term "Raynaud's Phenomena" will include all those vasospastic conditions which manifest the characteristic responses on exposure to cold. At the same time it must be realised that the recognition of the primary factor responsible must be acknowledged and, if possible, dealt with. Removal of such a factor would, of course, result in complete and permanent cure in BOTH the upper and the lower extremity.

However, there are a large number of cases in which there is apparently no other abnormality than the response of

/the digital

the digital vessels to cold. It is this group which for so long has defied efforts to produce a lasting cure.

After Royle (1924) had demonstrated the value of sympathectomy for vasospastic disorders, the operation of cervico-thoracic sympathectomy appeared to be the answer to the problem. The immediate results were good but subsequent study of the patients showed that relapse not infrequently occurred.

Comparison was made with the lower extremity, where late results were uniformly good. The operation was modified to become preganglionic and great results were expected. Unfortunately, observers were disappointed. No matter the type of operation, Raynaud's Phenomena still recurred in the upper extremities.

Further modifications of Royle's operation were tried. Newer theories were elaborated. Each theory and operation was developed and put to the test but recurrence of symptoms appeared unavoidable.

In an attempt to explain the poor late results, regeneration of the sympathetic was most prevalently held to be the responsible factor. In few cases, however, was it possible to demonstrate the re-establishment of anatomic pathways.

IT IS THE PURPOSE OF THIS PAPER TO ANALYSE THE RESULTS OF SYMPATHECTOMY OF THE UPPER EXTREMITY IN RAYNAUD'S PHENOMENA AS PERFORMED AT GROOTE SCHUUR HOSPITAL, AND TO DEMONSTRATE BY EXPERIMENTAL MEANS WHETHER REGENERATION OF THE SYMPATHETIC NERVOUS SYSTEM IS RESPONSIBLE FOR THE RETURN OF SYMPTOMS IN THE UPPER EXTREMITY.

II. THE SYMPATHETIC NERVOUS SYSTEM.

(a) HISTORY.

Galen (about 150 A.D.) was the first to offer the widely accepted interpretation of "sympathy" or "consent" between different parts of the body. This view pervaded physiologic thought until the beginning of the last Century. Galen enumerated seven pairs of cranial nerves. The description of the "sixth pair" of cranial nerves, given by Galen and religiously followed by all anatomists until, and including, Vesalius, grouped the vagus nerve and the ganglionated trunk of the sympathetic system as one, both anatomically and physiologically.

Etienne (1545) and later Eustachio (1552) first distinguished the vagus and ganglionated sympathetic trunk anatomically in the neck. Eustachio pictured the sympathetic component as arising within the cranium, a fallacy not corrected until 1727 by the work of du Petit.

Willis (1621 - 1675) recognised and illustrated the apparent union in lower animals of the cervical portion of the sympathetic trunk and the vagus nerve and their separate course in man. Willis, too, was one of the first to introduce into scientific thought the conception of "involuntary" as distinct from "volitional" movement.

Whytt (1751) extended greatly Willis' differentiation of animal motions into voluntary and involuntary movements and, without knowledge or any theoretical conception of a reflex action, emphasised the effective response to an affecting stimulus, dependent at least in part on the integrity of nerve connection.

du Petit in 1727 dealt the "death blow" to the proposed cerebral origin of the "intercostal" nerve (as Willis

/had designated

had designated the ganglionated sympathetic trunk). By careful dissection and then by experimental section of the vago-sympathetic trunk in the neck in dogs, du Petit gave the first accurate account of Horner's Syndrome. He distinguished clearly between the respiratory embarrassment due to vagal section and the ocular palsy due to paralysis of the cervical portion of the sympathetic trunk. It was a century-and-a-half before the full significance of du Petit's observation was realised. It was not until the time of Gaskell and Langley that it became clear and was proved experimentally that the only possible pathway from the central nervous system to the sympathetic ganglia is through the rami communicantes.

Johnstone in 1764 gave a remarkably accurate account of the gross appearance of the ganglia but leaned towards Winslow's (1732) view of semi-independence of the ganglionic system.

Meckel in 1751 gave the first clear account of what is now understood by the term "nerve plexus", and although he remarked that the bulk of the nerves leaving the ganglion was much greater than that of the entering nerves, he apparently did not suspect a possible origin within the ganglion of such emergent fibres. Meckel added the significant observation that many nerves of the sympathetic system, especially those leaving the ganglia, were redder and of softer texture than most other nerves, an early glimmering of the recognition of the non-myelinated nature of the fibres of the "grey rami".

In 1836 Valentin gave a detailed account of the sympathetic ganglia. He noted the difference between the white and grey rami communicantes and expressed the belief that the white rami arose from the spinal cord and passed to the sympathetic system.

/two years later.

Two years later Remak gave the first adequate description of the unmyelinated nerve fibres which he postulated arose from the ganglion cell bodies described by Ehrenberg in 1833. The true nature of Remak's fibres remained in dispute for many years, but were gradually accepted when Muller, Schwann and Henle confirmed Remak's observations. Remak's was one of the earliest clear descriptions of the anatomy of the white and grey rami communicantes.

In 1857 Meissner gave the first description of the submucous plexus of the intestinal tract and in 1864 Auerbach published his account of the myenteric plexus of the intestinal wall.

In 1862 Reissner observed that the fine nerve fibres were present in the anterior roots of the thoracic region in far greater numbers than elsewhere in the spinal segments.

After Muller in 1838 had recognised two kinds of muscle, striated and unstriated, Henle in 1840, noting that sympathetic fibres, apparently motor in nature, were distributed particularly along blood vessels, was led to the conclusion that the middle coat of arteries was muscular. Histologic proof was given by von Kolliker (1846).

Bichat in 1799 was the first to correlate the autonomic nervous system with the metabolic functions of the body. He also heralded the discovery of the vasomotor nerves - "..... the nerves of the ganglia are distributed everywhere to the circulatory system; they seem to exist for it and to belong to it exclusively. It is only with the arteries that they are introduced into the organs, or rather it is only to the arteries that they are distributed directly, no matter where they are. This constant connection between the nervous system of the ganglia and the circulatory system is observed even in the heart....."

/The first evidence

The first evidence of the vasomotor function of the sympathetic nervous system was demonstrated by Claude Bernard. In 1852 he described the increase in the blood flow and the temperature of the skin on the side of the head on which he had sectioned the sympathetic trunk in the neck.

This was confirmed in 1852 by Brown-Sequard who also demonstrated that sympathetic stimulation caused vasoconstriction and a decrease in the temperature of the skin in the area supplied. Wall in England and Budge in Germany confirmed this independently. Bernard (1862), Schiff (1862) and von Cyon (1868) showed the same vasoconstrictor action of the sympathetic supply to the upper limb.

After Ludwig (1851) had noted increased secretion of the saliva on stimulation of the chorda tympani, Bernard in 1858 showed that the blood of the submaxillary gland was under the control of two types of nerve fibres - the sympathetic, causing constriction of the arteries and diminution of blood flow, and the chorda tympani, stimulation of which gives vasodilatation and an increase of blood flow.

In 1876 Stricker demonstrated the vasodilator effect of stimulation of the dorsal spinal roots, and in 1880 Dastre and Morat produced evidence for the existence of vasodilator fibres to the mucous membrane of the gums and palate in the cervical portion of the sympathetic chain.

Gaskell in 1886 showed that the white rami communicantes were composed almost entirely of fine myelinated fibres and that they were clearly limited to the thoracic and upper lumbar segments. In the cephalic portion of the sympathetic chain the small medullated nerve fibres could be traced to the superior cervical ganglion and no further. Caudally, they formed the lumbo-sacral trunk, gradually decreasing in number until in the lower sacral regions they

/ultimately

ultimately disappeared. Laterally some fibres were traced through the sympathetic ganglia into the splanchnic nerves. Gaskell also noted medullated fibres of fine calibre in the second and third sacral segments as also in the spinal accessory, glossopharyngeal and chorda tympani nerves.

Gaskell was probably the first to postulate the existence of two antagonistic systems of nerves for the control of involuntary musculature and glandular secretion, one excitatory and the other inhibitory.

The differentiation of the two components of the autonomic nervous system is mainly due to Langley who termed the cranial and sacral outflow as parasympathetic. The thoraco-lumbar outflow constitutes the sympathetic proper.

After Hirschmann in 1863 and Heidenhain in 1872 had noted the effects of nicotine on stimulation of the sympathetic trunk in the neck, Langley and Dickinson in 1889 established that the vasodilator fibres for the pupil and the vasoconstrictor fibres for the ear end in cells in the superior cervical ganglion. By applying this discovery to other parts of the body, Langley was able to map out the cell stations and areas of distribution of most of the pre-ganglionic and postganglionic neurones which he thus named in 1893.

With the discovery of the elaboration of chemical substances, sympathin (Cannon) and acetylcholine (Loewi and Dale), at the terminations of the sympathetic and parasympathetic nerve fibres respectively, the first important links between the autonomic and the endocrine systems were forged.

/(b) ANATOMY AND PHYSIOLOGY

(b) ANATOMY AND PHYSIOLOGY.

1. Embryology.

The comparative anatomy of the sympathetic nervous system is not very well known. In the Petromyzon, the most primitive of the chordates, a vagal system can be distinguished and, as one ascends in the scale, portions of the sympathetic system gradually make their appearance. The autonomic system appears comparatively late and, of its three portions, the thoraco-lumbar outflow is the last to appear.

The chromaffin system is much more extensive in the lower vertebrates than in man and it undergoes a progressive reduction as one passes up the animal scale. With this reduction in the chromaffin system there is a progressive increase in the peripheral plexuses of the sympathetic system. The role of adrenalin apparently was the replacement of the postganglionic fibres by the distribution through the blood of a chemical substance. In the course of evolution the less exact has given way to the more precise and more highly differentiated method.

Kuntz (1922) and Jones (1937, 1939, 1941) consider that the peripheral neurones of the sympathetic system in the thoracic and abdominal region are derived mainly from the neural tube. Their work was performed on the chick and neuroblasts were said to leave the neural tube and enter into the formation of the sympathetic trunk.

Scott and Palmer (1932) outlined the embryonic development of the cells of the sympathetic system as being derived from the neural crests and ventral roots.

Woollard and Norrish (1934), too, considered that the neural crest was the source of origin of the cells of the sympathetic ganglia.

/Hammond.

Hammond and Yntema (1947), by removing the neural crest from the lumbar and thoracic regions of the chick, demonstrated that the peripheral sympathetic neurones in those regions arise from the neural crest.

The preganglionic column and its fibres differentiate in the absence of the neural crest and its derivatives. They emerge from the neural tube and complete an essentially normal pattern for a trunk sympathetic system devoid of peripheral sympathetic neurones. There is no evidence that cells migrate from the preganglionic column or ventral neural tube to form neurones of the sympathetic ganglia. Injury to the preganglionic centre, along with absence of sympathetic ganglia, is reflected in interruption or absence of the paravertebral trunk for one or more segments.

Thus it is from the neural crest that cells of the sympathetic ganglia and the chromaffin cells take origin. They arise from the same source as the dorsal ganglia of the cerebrospinal nerves. The neuroblasts which are proliferated from the neural crest become aggregated in a segmental manner, so that in the postganglionic system of the sympathetic the metameric arrangement is preserved. A segmental plan does not occur in the preganglionic system, for this part is restricted to the thoracic region of the cord. Its connections with the peripheral ganglia, therefore, show an overlapping.

The paravertebral ganglia extend right down to the coccygeal region and up into the neck. In the cervical region, however, although a strict segmental distribution undoubtedly occurred, there has been fusion of the ganglia into three main groups, forming the superior, middle and inferior cervical ganglia. The inferior cervical ganglion represents the fused seventh and eighth, and the middle cervical ganglion the fused fourth and fifth cervical ganglia,

/whereas the

whereas the superior cervical ganglion incorporates the upper four cervical ganglia.

Pick and Sheehan (1946) have pointed out that irregularity in the number of ganglia along the sympathetic chain is a familiar observation and is more marked in the lower thoracic and upper lumbar regions. There is apparently division of each primordial ganglionic mass into cranial and caudal portions.

The two portions may fuse together again (or never really separate), producing a single ganglion with connection to only one spinal nerve - this type is truly segmental and most commonly seen in man in the upper thoracic regions.

The caudal half of one primordial mass may fuse with the cranial half of the next lower, forming a ganglion with connections to two spinal nerves and is, therefore, not strictly segmental.

There may be a fusion of portions of more than two primordial masses. All combinations are possible, and therefore one can find all types of ganglia with connections to three or more spinal nerves. This is seen typically in the superior and inferior cervical ganglia.

One or both portions of the primordial mass may persist as a separate ganglion, thus producing additional ganglia or complete duplication.

A primordial mass, or a portion of it, may appear to be missing altogether, when the rami usually connected with it come directly off the sympathetic chain.

All these varieties can, therefore, be recognised if the ganglia are numbered in accordance with the distribution of the rami. This is the only method of determining the proper enumeration of the ganglia and of making a true comparison between general dissections.

/2. Central Representation

2. Central Representation.

The mechanisms which control the vessels are by no means so clear cut as those which control the heart. Two distinct influences constantly affect the blood vessels, the vasoconstrictor and the vasodilator mechanisms, which are partly nervous and partly chemical. The impulses concerned emanate from the central nervous system, especially from the medulla, where a vasoconstrictor centre has been described, although, as in the case of the cardiac centres, these may really be the apices of reflex arcs.

The conception of special centres in the brain controlling blood vessels was first suggested by Schiff (1855) on the basis of the effect of section of the spinal cord. The workers of Ludwig's laboratory found that, even after all the brain above the medulla was removed, they still obtained a rise of blood pressure on stimulating the central end of the sciatic nerve. (Dittmar - 1870).

1. Cortex.

There is no unanimity in the literature on the question of the sympathetic system being represented in the cortex. In the monkey, stimulation of the premotor area produced cardiovascular effects and increase in intestinal peristalsis.(Watt and Fulton - 1934, Kennard - 1934).

Hoff and Green (1936) and Green and Hoff (1937) have concluded from animal experiments that the cortex may influence the cardio-vascular system depending on the needs of the animal in relation to the external environment.

Both Clymer (1870) and Maxwell (1902) have reported cases who seem to have a voluntary control over their sympathetic functions. Lindsley and Sassaman (1938) reported on a patient who was able to produce voluntary pilo-erection, with an increase in heart rate and blood pressure.

/Electrical

Electrical potential recordings show changes over the premotor area only during the period of peripheral autonomic discharge.

Vasomotor disturbances have long been noted in cases of hemiplegia. Eulenberg and Landois - 1876, Gowers - 1888, Pilcher, Wyatt and Carney - 1941 demonstrated unilateral sympathetic over-activity following a large infarct blocking the left middle cerebral artery. This is interpreted as a release phenomenon of cortical inhibitions.

Bucy (1935) observed a woman who, following a vascular accident, probably in the left internal capsule, showed complete disappearance of the right brachial and radial pulses. The limb was cyanotic and cold at first. Recovery was complete.

That emotional disturbances and mental strain cause a decrease in peripheral blood flow, which is dependent upon the integrity of the sympathetic pathways, was shown by Goetz (1943, 1946).

Although most of the work on the question of sympathetic representation in the cortex has resulted from animal experimentation, there appears to be no doubt that in man, too, the cortical centres influence the function of the sympathetic nervous system.

ii. Hypothalamus.

With regard to the evidence of sympathetic representation within the hypothalamus and wall of the third ventricle, numerous papers have appeared. Animal experiments have again been the mainstay of physiologists. Direct stimulation of the various posterior nuclei has been performed and all aspects of sympathetic activity noted. (Ranson and Magoun - 1933, Hare and Geohegan - 1939,

/Walker - 1940

Walker - 1940, and Pitts et al - 1941).

All the sympathetic activity resulting from stimulation of the higher centres is dependent on the presence of the intact thoracic sympathetic chain and is abolished by resection or the injection of a sympathetic paralysant.

Beattie in 1932 postulated a vasoconstrictor centre in the caudal, and a vasodilator centre in the oral part of the hypothalamus.

White in 1940 found, while operating on five conscious patients, that electrical stimulation of the paraventricular nucleus of the hypothalamus caused a rise in blood pressure and acceleration of the heart rate. Bradycardia, however, resulted from stimulation of the anterior hypothalamus near the preoptic nucleus.

Numerous clinical observations of tumours or other lesions which compress or destroy the walls of the third ventricle support the experimental evidence. Peet and Kahn (1936) report a case of "Raynaud's Phenomena" occurring in a patient with a tumour of the hypothalamus. The "Raynaud's Phenomena" consisted of severe vasoconstriction with cyanosis and sweating of the extremities. Penfield (1929) reported a case of tumour of the third ventricle, with attacks of what he called "Diencephalic autonomic epilepsy". This included cutaneous vasodilatation, salivation, sweating, pilomotor activity, dilatation of pupils, tachycardia, rise in blood pressure and spasm of sphincters.

There appears to be evidence of two distinct mechanisms present - one in the posterior part of the hypothalamus causing a co-ordinated response of sympathetic outflow and the other in the anterior part producing a similar response of parasympathetic outflow.

The whole object of these mechanisms appears to be

/towards the

towards the maintenance of a constant internal environment. As emphasised by Goetz (1947), the cortex exerts a controlling or inhibitory influence upon these mechanisms.

The close relationship of the hypothalamus to both the sympathetic nervous system and to the pituitary gland, and thus to the entire endocrine system, must continually be borne in mind.

iii. Medulla.

In 1916 Ranson and Billingsley investigated the problem of higher centres in the medulla. They examined the floor of the fourth ventricle with stimulating electrodes. Their work was performed on cats. They found two points - one of which gave a definite rise of blood pressure and the other a fall. These two points were no more than 3 mm. apart. The pressor point was on the lateral lip of the ala cinerea.

These findings of a vasoconstrictor and a vasodilator centre were confirmed by Alexander in 1946.

It is likely that these centres are in close relation to the centre controlling cardiac activity. The proximity of the vasomotor centre to the respiratory centre is well recognised. This is well demonstrated by the respiratory fluctuations imposed upon the vasomotor impulses, and was well shown in the plethysmographic records of the peripheral blood flow. (Goetz - 1943, 1946).

iv. Spinal Cord.

In the frog Goltz (1864) showed that, even after the medulla is severed from the spinal cord, the vascular tone might recover, but that it was lost after the cord was destroyed. In the dog he also demonstrated that, if the cord in the upper lumbar region was cut, the temperature of the

/lower limbs

lower limbs became higher than that of the upper because of dilatation of vessels. Gradually, however, the vessels became normal again, but again they dilated if the lumbar cord was destroyed. This work suggests the existence of subsidiary vasomotor centres in the spinal cord. Further evidence supporting this view is that after the cervical cord has been cut section of the splanchnic nerve may cause a further fall of blood pressure.

The efferent vasoconstrictor pathway has been studied by cutting or stimulating it at various points. A number of early workers had described the sympathetic as taking origin from all the spinal nerves. The idea that the white rami were absent from the upper and lower regions of the cord was first put forward by Beck in 1846 on the basis of anatomical dissections of man.

In 1883 Gaskell suggested that the vasomotor (meaning the vasoconstrictor fibres) took origin from the lateral horn of the spinal cord and this was later confirmed by Anderson.

Vasomotor, sudomotor and pilomotor fibres from the higher centres pass down along the extrapyramidal tracts in the posterior longitudinal fasciculus and the vestibulospinal tracts into the antero-lateral columns of the spinal cord. There, synapses are established with the ganglion cells in the lateral horns, constituting the spinal sympathetic motor centres. The axons of these ganglia in the lateral horn are medullated and proceed to the corresponding sympathetic paravertebral ganglia via the anterior roots and the rami communicantes to synapse with ganglion cells in the paravertebral ganglia. These white (medullated) fibres are known as preganglionic fibres. The axons of the ganglion cells in the paravertebral ganglia are non-medullated. These are

/termed grey

termed grey fibres and reach the effector organs, either by joining the spinal nerves to the somatic regions or by joining the blood vessels to the splanchnic (visceral) areas.

In man the sympathetic centres in the lateral horn of the spinal cord extend only from Th.1 to L.2. Harman in 1898 showed that the superior limit is at the level of the first thoracic nerve. In some few cases the limit may be extended to the eighth cervical nerve. This variation appears to be so according to the fixation of the brachial plexus. As the plexus moves up one segment, the preganglionic outflow moves up to C.8. Should the plexus be post-fixed the second thoracic ganglion may become the highest spinal outflow. Similar observations were made by Foerster (1936) and Goetz and Marr (1944).

No sympathetic outflow apparently occurs through the anterior roots in the cervical regions, nor in the lumbar or sacral regions below L.2. The preganglionic fibres to the cervical ganglia reach them along the sympathetic cord via the first thoracic ganglion. In the lumbar and sacral ganglia the preganglionic fibres pass by way of L.2.

Pick and Sheehan in 1946 confirmed the thoraco-lumbar outflow in man as being derived from Th.1 to L.2. They, however, noted that the number of fine myelinated fibres within grey rami has been greatly underestimated. They occurred in great numbers in C.7 and C.8. They found that fine myelinated fibres were present to some extent in all grey rami.

/3. <u>Sympathetic Outflow</u>.

3. Sympathetic Outflow to the Upper Extremity.

1. Preganglionic.

In the upper extremity the sympathetic nervous system has been found by the surgeon to be apparently anomalous in its devious origins and ramifications. Anatomic dissection does not suffice to indicate the physiologic pathways of the sympathetic nervous system. Variations occur not only in different individuals but also between the two sides in the same individual.

Much experimental work has been done on this problem and the position is still far from clear. The origin of the preganglionic fibres to the upper extremity is still a matter of considerable dispute.

Sheehan and Marazzi (1941) recorded electrical activity of peripheral nerves during stimulation of anterior nerve roots in the monkey, and concluded that the preganglionic outflow to the upper extremity in the monkey is limited to roots Th.4 to Th.8.

Also working on monkeys, Ascroft found segmental levels were Th.3 to Th.9.

Geohegan et al (1942) used the skin resistance method and stimulated ventral roots in the monkey. They found that preganglionic fibres to the monkey's hand emerge through ventral roots Th.4 to Th.10. The preganglionic fibres to the sympathetic chain leave the cord over the first four thoracic ventral roots. They also found that there is asymmetry of the preganglionic outflow on the two sides of the same animal.

Kuntz and Dillon (1942), on the other hand, using the plethysmograph, demonstrated that, in the cat, and also the monkey, complete sympathetic denervation of the upper extremity cannot be accomplished by any operative procedure,

/which leaves the

which leaves the cervico-thoracic sympathetic ganglion with its grey communicating rami intact and does not interrupt the preganglionic components of the first thoracic nerve. They did this by demonstrating vasoconstriction following extirpation of the second and third thoracic segments of the sympathetic trunk. The first thoracic nerve includes preganglionic components which are involved in the sympathetic innervation of the upper extremity.

Thus, in the experimental animal, there is no unanimity on the upper level of the outflow of sympathetic fibres to the upper extremity. It is this upper level which is of the utmost importance.

Pick and Sheehán (1946) have pointed out that, although the thoraco-lumbar outflow in man is derived from Th.1 to L.2, as determined by the quantity of myelinated fibres, the number of these fine myelinated fibres has been greatly underestimated. Great numbers occurred in C.7 and C.8 and myelinated fibres were present to some extent in all grey rami.

In the series of monkeys sympathectomised during the past twelve months, direct stimulation was applied to the sympathetic trunk and ganglia. The plethysmograph was used to record evidence of vasoconstriction. In all, stimulation applied to the stellate ganglion resulted in constriction. In only one specimen, monkey"G", was stimulation applied cephalad to the stellate ganglion. In this animal, after the stellate ganglion had been removed, the cervical sympathetic was defined and identification confirmed by observing the effect of stimulation on the pupil. Stimulation of the cervical sympathetic, at a point just above the sixth cervical vertebra, did not result in vasoconstriction observed plethysmographically. Each stimulation at this point was accompanied by pupillary dilatation. Stimulation of the caudal end of the sympathetic trunk, i.e. at the

/fourth

fourth thoracic ganglion, had no effect on the hand volume.

In monkey "F", before the stellate ganglion was removed, all connections, excepting the two branches encircling the subclavian artery and a large ramus from the first thoracic nerve, were severed. Stimulation of this latter ramus produced both vasoconstriction of the upper extremity and dilatation of the pupil. This ramus was the white ramus of Th.1. Once this fibre was divided, stimulation failed to produce any evidence of vasoconstriction. This confirms the impression of Kuntz and Dillon.

The lower limit of sympathetic supply to the upper extremity varied. In three specimens no vasoconstriction occurred below Th.4. In one specimen it was not until the seventh thoracic ganglion was reached that constriction did not occur.

Thus, in the monkey, the upper limit of the sympathetic supply to the upper extremity appears to be the first thoracic segment. It is not, however, improbable that some of the myelinated fibres contained in the cervical segments, as demonstrated by Pick and Sheehan, may also play some part in the sympathetic innervation.

Foerster (1936) observed that Th.2 was the upper limit of the sympathetic supply to the upper extremity in man. Smithwick (1941) believes that both Th.2 and Th.3. contribute preganglionic fibres to the arms in man.

Hyndman and Wolkin (1941) found abundant thermoregulatory sweating of the whole upper extremity after anterior rhizotomy in which only the second thoracic root was left intact.

Atlas (1941) removed the second intercostal nerve, the second thoracic ganglion and all rami communicantes

/attached thereto

attached thereto on one side and by accident removed a like amount of the third on the other side. On the side that the second ganglion was removed the limb was found to be sympathectomised, but not so on the side from which Th.3 had been removed.

Hyndman and Wolkin (1942) concluded that removal of only the second thoracic sympathetic ganglion results in as complete a sympathectomy as does removal of the inferior cervical and upper two thoracic ganglia.

Fulton (1943) considers that it is highly unlikely that Th.1 makes any contribution to the sympathetic innervation of the upper extremity.

Goetz and Marr (1944) claim that removal of the second thoracic ganglion completely sympathectomises the upper extremity. Immediately after operation plethysmography reveals absence of vasomotor tone and complete anhidrosis of the upper extremity is present. The late results of their cases seem to indicate that removal of the second thoracic ganglion only does not produce a lasting sympathectomy. Goetz (unpublished data), therefore, extended the operation to include the third thoracic ganglion. Later, at his suggestion, the second, third and fourth thoracic ganglia were removed in all sympathectomies of the upper extremity.

Kuntz, Alexander and Furculo (1938) state that the preganglionic neurones involved in the sympathetic innervation of the upper extremity are located in the upper thoracic region of the spinal cord, beginning with the first thoracic segment and extending downward at least as far as the third or fourth. This statement is based on their work in the cat and the monkey.

Ray and his co-workers (1943) used the skin resistance method to determine the exact outflow from the spinal

/cord.

cord. The tests were based upon the established fact that sympathetic nerves leave the cord via anterior spinal roots and that faradic stimulation of these roots causes sympathetic activity, one effect of which is a change in the electrical resistance of the skin in the area innervated.

The cases were those in which the cervico-thoracic region of the cord was exposed.

In sixteen patients in whom the study was made, principally directed toward the hand, it was found that there was a variation in the upper and lower levels of the sympathetic outflow within the limits of the first thoracic and tenth thoracic segments. However, in over 90 percent. of cases the outflow was from the second, fourth and fifth thoracic segments.

After having noted the ease with which the sympathetic chain was stimulated in the monkey, the sympathetic trunk and ganglia were stimulated at operation in one of the cases in the present series. Vasoconstriction was observed plethysmographically.

The sympathetic trunk was exposed by open thoracotomy as described by Goetz and Marr (1944). The upper thoracic ganglia were defined by blunt dissection and electrodes placed on the ganglia. The stellate, second and subsequent ganglia were thus stimulated and the plethysmographic record observed. Vasoconstriction resulted on stimulation of the fourth thoracic ganglion and at all points of the chain cephalad, as far as and including the stellate ganglion. It is impossible to stimulate above the stellate ganglion via the thorax. Thus, whereas the lower limit of the sympathetic innervation to the upper extremity is easily demonstrable, the upper limit has not been defined.

/The reaction

The reaction of the pupil was observed whilst stimulation was being performed. Stimulation of the stellate ganglion was followed by dilatation. But a similar dilatation occurred on stimulation of the second thoracic ganglion. This ganglion was included in the tissue removed. Postoperatively a Horner's Syndrome was present which, however, had completely disappeared by the eighth day.

In the majority of cases, removal of the second thoracic ganglion will completely denervate the upper extremity of sympathetic fibres (Hyndman and Wolkin - 1942, Goetz and Marr -1944). In less than one out of ten an outflow occurs from the first thoracic nerve and in these cases removal of the second thoracic ganglion will not completely sympathectomise the upper limb. (Ray et al - 1943).

Goetz and Marr (1944) and Goetz (1948) have demonstrated that, by removal of the thoracic sympathetic below Th.1 43 percent. of cases show abolition of thermo-regulatory sweating of the face and neck. In the remaining 57 percent. the skin structures of the face and neck were not denervated. In these patients Th.2 was not the highest source of sympathetic outflow. Although there was this difference in the sweating fibres in these cases, no difference occurred in the sympathetic supply to the pupil. In all cases in which the sympathetic was removed below the stellate, Horner's Syndrome was absent. This indicates that the central connection of the oculo-pupillary apparatus via Th.1 is constant.

However, it is possible for Th.2 to supply some fibres to the pupil. Horner's Syndrome was present in one case for only eight days after removal of the second thoracic ganglion and it is likely that the bulk of the fibres to the pupil arose normally from Th.1.

/it is possible

It is possible to determine whether the limb has been completely sympathectomised. In the monkey, after sympathectomy had been performed, the caudal end of the sympathetic trunk, intercostal nerves and the bed from which the sympathetic had been removed were all stimulated, and the vasomotor responses in the limb were recorded plethysmographically.

This method was applied in the patient mentioned above. No vasoconstriction was noted on stimulation of the caudal end of the sympathetic, intercostal nerves, or sympathetic bed. The sympathectomy thus appeared complete.

Using this method it is thus possible to determine at the time of operation, firstly, the extent of sympathetic supply to the upper extremity and, secondly, the completeness of operation.

In some cases one of the communicating rami which connects the cervicothoracic ganglion with the eighth cervical nerve bifurcates and sends one division into the low middle cervical ganglion. This ramus is made up mainly of unmyelinated fibres of small calibre which are postganglionic. In some instances small myelinated fibres are present among the unmyelinated ones. These myelinated fibres probably are mainly preganglionic fibres which in these cases emerge through the eighth cervical nerve. This communicating ramus, therefore, constitutes a pathway through which, in certain cases, some preganglionic fibres may reach the low middle cervical sympathetic ganglion without traversing the cervicothoracic ganglion. (Kirgis and Kuntz - 1942).

The first sympathetic trunk ganglion below the cervicothoracic, i.e. the second thoracic ganglion, is located at the level of the second thoracic nerve. In some instances, however, the second thoracic sympathetic ganglion is incorporated in the stellate ganglion.

/The second

The second thoracic nerve is connected with the second thoracic sympathetic ganglion of the sympathetic trunk by a white and a grey ramus.

The second thoracic nerve is not commonly regarded as contributory to the brachial plexus. But in a large percentage of cases an intrathoracic ramus of the second thoracic nerve joins the first thoracic nerve. It may join only the intercostal ramus of the first thoracic nerve or only the brachial plexus or it may contribute fibres to both. (Kuntz - 1927).

Kuntz further observed that, in some cases, a grey ramus from the second thoracic sympathetic ganglion or the sympathetic trunk was traced directly into the ramus connecting the first and second thoracic nerves, or a ramus from the stellate was traced into this ramus. In all cases in which a grey ramus was traced from the second thoracic ganglion or the sympathetic trunk directly into the ramus joining the first thoracic nerve, one or more communicating rami also joined the second thoracic nerve. In a few instances a small ramus was traced into the first thoracic nerve directly from the second thoracic ganglion, or the communicating ramus connecting this ganglion with the second thoracic nerve.

Microscopy of the intrathoracic ramus joining the first and second thoracic nerve revealed that myelinated fibres occur there more frequently than they do in sections of spinal nerves distal to the communicating rami. Thus, the intrathoracic ramus connecting the first and second thoracic nerves, which is present in man in a large percentage of cases, contains sympathetic fibres. Whenever this ramus joins the first thoracic nerve proximal to the origin of the first intercostal nerve it constitutes a pathway through which sympathetic fibres which leave the sympathetic trunk below the stellate ganglion, enter the brachial plexus.

/The third thoracic

The third thoracic ganglion is located at the level of the third thoracic nerve. It is connected with this nerve by a white and a grey communicating ramus.

A ramus arising from the third thoracic nerve just distal to the junctions of the communicating rami with this nerve and joining the second thoracic nerve, was demonstrated bilaterally in fifteen and unilaterally in eighteen of the forty-four cadavers examined by Kuntz and Kirgis (1942). In six of the remaining eleven cadavers, in which no direct communication between the third and second thoracic nerves could be demonstrated, a ramus arising from the third thoracic nerve either joined the second thoracic sympathetic ganglion or the sympathetic trunk just below this ganglion. In all cases in which the ramus arising from the third thoracic nerve joined the second, the junction occurred in proximity to the junction of the grey communicating ramus with the latter nerve or took place directly with its grey communicating ramus, and consequently, in proximity to the origin of the ramus of the second thoracic nerve which joined the first. In some cases the ramus arose from the third thoracic nerve and joined the second at more than one point. In a few instances one branch could be traced directly into the ramus arising from the second thoracic nerve, which joined the first. The ramus in question, arising from the third thoracic nerve, lay closely applied to the anterior surface of the third rib and the intercostal muscle and was embedded in the loose areolar connective tissue which lay in relation to the sympathetic trunk. Instead of joining the second thoracic sympathetic ganglion or the sympathetic trunk below the latter ganglion, it may be completely concealed by the connective tissue. (Kuntz and Kirgis - 1942).

/ii Postganglionic

ii. Postganglionic.

Sympathetic fibres which supply the upper extremity leave the sympathetic trunk mainly through grey communicating rami which arise from the inferior and middle cervical and second thoracic ganglia and join the nerves which make up the brachial plexus. These ganglia, as well as the upper thoracic ganglia, are extremely variable.

The topography of the middle cervical ganglion is very uncertain. It is usually assigned to a place where the cervical sympathetic chain crosses the inferior thyroid artery opposite the sixth cervical vertebra. It is, however, a fluctuating quantity and considerable variation occurs in the origin and course of the rami to the fifth and sixth cervical nerves which are usually attributed to it. (Woollard and Norrish - 1934).

Both Potts (1925) and Axford (1927) state that the middle cervical ganglion may be of two types:-

(1) The ganglion lies in close association with the inferior thyroid artery at about the level of the sixth cervical vertebra.

(2) The ganglion lies on the ventral side of the vertebral artery at about the level of the seventh cervical vertebra.

The former or high type of ganglion gives rami communicantes constantly to the fifth and sixth cervical nerves. The rami communicantes from the low type of ganglion are distributed most frequently to the fifth and sixth cervical nerves, but there is some variation in that rami may proceed from it to the fifth cervical nerve alone or to the fifth, sixth and seventh cervical nerves.

When this ganglion is absent, or lies in close proximity to the inferior cervical ganglion, the fifth and sixth cervical nerves derive their rami direct from the sympathetic trunk. (Potts - 1925, Kuntz - 1927).

/The inferior

The inferior cervical ganglion is commonly situated in the region of the level of the neck of the first rib, but may occupy a slightly lower level. The ganglion supplies rami to the seventh and eighth cervical and first thoracic nerves. The rami to the fifth, sixth and seventh nerves may be on the surface of the scalenus anterior or may wander among its fibres, depending on whether they lie in front of, under cover of, or pierce the muscle. (Potts - 1925).

However, Kuntz (1927) states that a discrete, inferior cervical sympathetic ganglion occurs but rarely, if at all, in man. The inferior cervical ganglion is partially or entirely fused with the first thoracic ganglion in 80 percent. of cases. All degrees of fusion can be seen. A complete union occurs in only about 50 percent. (Sheehan - 1933).

Most often it is found that an elongated ovoid mass is situated in front of the neck of the first rib and this mass, when traced upwards to the lateral angle between the vertebral artery and its origin from the subclavian, emits a stream of fibres in which one or more small ganglion masses are entangled. The lower pole of the ganglionic mass leads directly downwards and backwards to the second thoracic ganglion, which lies opposite the medial extremity of the first intercostal space and usually extends to the upper border of the second rib. (Gray's Anatomy).

The stellate ganglion which is commonly located in the interval between the eighth cervical and first thoracic nerves, is usually connected to the first thoracic nerve by two communicating rami, with the eighth cervical by two, with the seventh cervical by one and sometimes with the sixth cervical by one. (Kirgis and Kuntz - 1942).

The white ramus communicans from the first thoracic nerve enters the inferior cervical ganglion as a rule.

/It sometimes

It sometimes enters the first thoracic ganglion. It may enter either the upper or the lower part of the inferior cervical ganglion, most often into the lateral aspect of the lower part, and always at some distance (1 - 5mm.) below the origin of the grey rami communicantes to the cervical nerves. Traced backwards it courses almost directly outwards for about 1cm. and joins the first thoracic nerve on its anterior aspect where the nerve is crossing anterior to the neck of the first rib. Its direction, though principally outwards, is also slightly backwards, and, as it enters the upper part of the ganglion, courses slightly downwards; it courses slightly upwards on entering the lower part of the ganglion. It joins the nerve at a point some distance lateral to the point of junction of the corresponding grey ramus. It is relatively longer than the grey ramus and it lies anterior to the superior intercostal artery.

The opinion that the vascular route is used by sympathetic fibres has diffused widely following the work of le Riche. Actual observation discloses the penetration of the spinal nerves by rami; it shows fibres from peripheral nerves joining blood vessels - branches of vascular distribution. Numerous nerve fibres, in the form of fasciculi, running for considerable distances, can also be observed in the adventitia of blood vessels; and finally in the tunica media a continuous nerve plexus can be seen extending throughout the whole of the vascular tree.

The vascular tree from the aorta to the periphery appears to be supplied with vasomotor nerves in two ways. (Woollard - 1926). In the adventitia of the aorta there are large bundles of nerve fibres which come direct from the adjacent ganglia of the sympathetic trunk. These bundles are composed almost entirely of non-medullated nerves. This forms a fine network which gives complete continuity throughout the vascular tree.

/This double

This double mode of innervation had already been noted by Kramer and Todd (1914). They observed that the subclavian and axillary arteries differ from the other arteries of the arm in receiving a nerve supply direct from the sympathetic chain. All other arteries in the upper limb obtain their nerve supply from sympathetic filaments which have travelled along the spinal nerves and which are distributed to the various blood vessels at irregular intervals. The distal and peripheral vessels, more particularly those of the hand, receive nerve filaments at more frequent intervals than do the proximal channels. The distribution of nerves to vessels corresponds roughly with the distribution of nerves to the muscles and skin.

The continuous plexus in the media of blood vessels is, however, unlike a conducting system. It gives off peri-cellular endings to the unstriped muscle fibres. Impulses which enter this plexus extend over a small area and then die out Though its appearance suggests continuity, the arrangement is of such a nature that its purpose is to subserve a restricted portion of the vascular tree, and experiment shows that impulses soon die out within this area and are not transmitted for any distance upwards or downwards. (Woollard and Norrish - 1934).

That capillaries are accompanied by nerves was shown by Beal (1860). The fibres are fine and non-medullated. They belong entirely to the sympathetic system and are continued on to the capillaries from the arterioles. Definite endings in the capillaries, however, are not found. (Woollard - 1926).

Sanders, Ebert and Florey (1940) studied capillary contraction and were unable to find evidence to support the existing view that Rouget cells participate in this process. They report that capillaries contract independently of the Rouget cells. They were able to produce contractions at will by stimulating the peripheral end of the cut cervical portion of the sympathetic trunk. They conclude that these contractions are under the control of the sympathetic nervous system.

/The vasoconstrictor

The vasoconstrictor fibres are recognised to be exclusively sympathetic. It can be stated further that all vasoconstrictors are sympathetic postganglionic fibres and there is no other source of supply than these.

They leave the spinal cord by the ventral nerve roots and join the chain of sympathetic ganglia, in which they have their cell stations. So far as the supply to the limb is concerned, physiological evidence goes to show that the vasoconstrictor fibres controlling the arterioles travel with the peripheral nerves. Section of such nerves causes vasodilatation; stimulation produces vasoconstriction. Some observers have found bundles of nerve fibres running along the larger blood vessels and others have described small bundles of fibres approaching the vessels from the adjacent peripheral nerve trunks.

It appears that the smaller arteries and arterioles are supplied by sympathetic postganglionic fibres which reach the vessels by way of the peripheral nerves to the limb. (Bancroft - 1898).

(c) SYMPATHECTOMY.

Jonnesco (1897) had called attention to the fact that resection of the stellate ganglion with or without resection of the middle and upper cervical ganglia was first done, in 1896, for epilepsy and exophthalmic goitre, and later by other surgeons for migraine and glaucoma. Although operations on the sympathetic nervous system had been performed as early as this, Jaboulay (1893) had previously suggested periarterial sympathectomy for trophic and gangrenous diseases of the extremities.

It was not until le Riche (1913) became interested in this field that the operation gained any prominence. Periarterial sympathectomy was popularised by le Riche and the procedure has been employed on many occasions. Results, however, of this procedure have been conflicting and, in the main, disappointing.

/Kramer

Kramer and Todd (1914) and Potts (1914) all pointed out that only the subclavian and femoral arteries received sympathetic vasomotor fibres directly from the ganglia. le Riche's conclusions were, therefore, unsound anatomically. Nevertheless, le Riche and Fontaine (1928) still held that periarterial sympathectomy was indicated and moreover claimed successful results.

The work of le Riche and his followers provided a great stimulus to the surgery of the sympathetic nervous system. Thus Bruning (1923), Hunter (1924) and Royle (1924) with Adson and Brown (1925) and Davis and Kanavel (1926) were all responsible for the interest in the surgical possibilities in the treatment of vascular diseases of the vasoconstrictor type.

Royle (1924) whilst treating spastic paralysis by sympathetic ramisection noted that the leg on the operated side was brighter in colour and was warmer than the normally innervated extremity.

In those operations on the sympathetic nervous system for epilepsy, etcetera, the stellate ganglion was removed. However, the middle and upper cervical ganglia were, often as not, included in the operation. Following a suggestion by Frank, Jonnesco modified the operation for the relief of angina pectoris.

In 1924 Royle modified the Jonnesco operation still further. He suggested ganglionectomy (stellate) and section of the sympathetic trunk below the first thoracic nerve. Royle used an anterior approach for his sympathectomies. Royle, however, pointed out the anatomical dangers of the anterior approach and noted that failures of this operation were due to incompleteness of the manoeuvre. In an attempt to minimise the operative

/danger

danger and thus prevent incomplete denervation, Adson and Brown (1929) developed the posterior approach.

Prior to this, however, Kuntz (1927) had pointed out that the second thoracic ganglion contributes grey fibres to the first thoracic spinal nerve as well as to the second thoracic nerve, which often contributes to the lower trunk of the brachial plexus.

Even at this early stage it was obvious that sympathectomy of the upper extremity did not produce the same lasting denervation of lumbar sympathectomy for the lower extremity. This explains Royle's observations on the dangers of the anterior approach and the consequent incompleteness of operation.

Adson and Brown's posterior approach was developed to obviate this difficulty and at the same time they confirmed Kuntz's observation of the intrathoracic ramus from the second thoracic ganglion to the first thoracic spinal nerve. This communicating ramus was held to be the reason for failure of operation in Royle's cases. They extended the operation to include the second thoracic ganglion. Removal of this ganglion would ensure, therefore, that Kuntz's nerve be removed at operation. Their procedure, therefore, was to remove the inferior cervical, first and second thoracic ganglia and intervening sympathetic trunk.

The results of Adson and Brown's method of sympathectomising the upper extremity were no better than those obtained by cervico-dorsal sympathectomy. The theory of sensitisation was then elaborated in order to explain relapses after sympathectomy of the upper extremity.

Meltzer and Meltzer (1903), Meltzer and Auer (1904) had observed that the arteries in the rabbit's

/ear after

ear after sympathectomy are intensely constricted for hours after subcutaneous injection of adrenaline. Smithwick, Freeman and White (1934) showed the same intense vasoconstriction in denervated arteries after adrenaline. These same authors suggested that the adrenal can secrete sufficient adrenaline in response to cold, emotion, etcetera to account for the failures of sympathectomy. They found that this sensitisation to adrenaline manifests itself on degeneration of the postganglionic neurones and lasts as long as sympathectomy is complete. Simeone (1937) confirmed that with re-establishment of vasomotor tone the phenomenon disappears.

Hampel (1935) and Grant (1935) showed that after preganglionic sympathectomy, the response to circulating adrenaline is less than half that found after degeneration of the postganglionic neurones. White, Okelberry and Whitelaw (1936) confirmed the apparent difference between pre- and post-ganglionic sympathectomy.

This hypersensitivity to circulating adrenaline after post-ganglionic section of the sympathetic supply to the upper extremity was the suggested reason for the failure of cervico-dorsal sympathectomy for Raynaud's Phenomena of the upper extremity. The good result obtained by lumbar sympathectomy for Raynaud's Phenomena of the lower extremities was explained by the fact that section of the lumbar chain, as done in most clinics, constitutes a preganglionic section. It was felt, therefore, that preganglionic sympathectomy of the upper extremity should be performed.

Accordingly, preganglionic sympathectomy of the

/upper

upper extremities was thus devised. Telford (1938) divided the thoracic ganglionated cord below the third thoracic ganglion. The rami which enter the second and third thoracic ganglia are sectioned and the upper end is slung to the scalenus anterior muscle and is either ligatured or silver clips are put on it to prevent regeneration. Telford's operation was performed via an anterior approach.

Smithwick (1937) sectioned the thoracic sympathetic trunk below the third thoracic ganglion and the communicating rami to the second and the third thoracic ganglia. The divided trunk was sutured to the muscles to prevent regeneration. Smithwick claimed that in this way all possible sympathetic connections to the brachial plexus were removed, except those which might be contained in the first thoracic nerve, section of which would give motor and sensory paralysis in the arm.

Whereas initially Smithwick considered that the above procedure would be sufficient, he further modified the operation. His earlier cases showed what appeared to be incomplete division and others appeared to show regeneration. Following this, extra-spinal root section was carried out - the second and third intercostal nerves were resected from the lateral portion of the operative field inward, dividing the posterior and anterior roots separately at a point just proximal to the posterior root ganglion. (Smithwick - 1940). This, Smithwick claimed, ensured division of the white rami communicantes as the anterior roots were always sectioned proximal to their origin.

The operation was further modified and termed intraspinal root section. The anterior root was divided by separating the attachment of the arachnoid and the root gently teased out. The healing of the meninges would tend to further guard against regeneration. The immediate

/effects

effects were excellent but the late results showed a return of vasoconstriction which was usually delayed as compared with ramisectomy.

It was obvious from the foregoing that a new factor would arise to explain the poor late results of sympathectomy of the upper extremities, as compared with the lower limbs - REGENERATION. Originally the divided end of the sympathetic chain had been buried either in the scalenus anterior muscle (Telford - 1938) or in the posterior group of muscles (Smithwick - 1940). To further guard against regeneration, ligation of the distally divided end of the sympathetic trunk was started. A further procedure was to cover the decentralised second and third thoracic ganglia and intervening trunk with a silk cylinder or cellophane.

The purpose of this manoeuvre was to prevent regeneration. White and Hamlin (1945) observed that regenerating fibres from the fourth thoracic ganglion or from the central stumps of the second and third intercostal nerves were apparently able to bridge the gap. The authors suggested the use of a tantalum sleeve and closing its lower end by crushing in a haemostat. They claim that regrowth should be prevented more effectively by this method.

The poor results of sympathectomy of the upper extremity are apparently due to regeneration. Simmons and Sheehan (1939) have observed that, theoretically, it is more difficult to visualise regeneration after ganglionectomy. If all the postganglionic cell stations to the arm have been removed at operation then either preganglionic fibres grow up and pass directly into the brachial plexus, or what appears to be more likely, postganglionic fibres whose cell stations are situated below the level of excision, regenerate

/through the

through the scar tissue to reach the nerves of the arm.

de Takats (1940) felt that preganglionic sympathectomy as practised by most surgeons would not result in a lasting sympathectomy. In order to make the removal as complete as possible he suggested extending the excision upward to include the middle or intermediate cervical ganglion or, if this is invisible, to strip the vertebral artery. Caudalward the third thoracic ganglion is included. de Takats claimed that these results are better than the preganglionic method.

At Groote Schuur Hospital, particularly after the work of Goetz and Marr (1944), the second thoracic ganglion only was removed or cauterised via the thoracoscope. All the cases operated on in this way had fairly good immediate results. The late results, however, indicate that there is complete or very nearly complete return of vasomotor tone.

The second thoracic ganglion could be removed in several ways. Thus Goetz and Marr (1944) suggested endoscopic cauterisation of the ganglion. The difficulties of this manoeuvre, however, are considerable. Not infrequently numerous adhesions are present adding considerably to the difficulties of visualisation of the sympathetic chain.

The same authors suggested and carried out removal of the second ganglion by open thoracotomy. Removal of the second or third rib by means of an anterior skin incision provided a fairly easy exposure of the ganglion. Apart from the results of sympathectomy by this method, an unsightly scar is left just above the breast. The psychological and cosmetic effect is considerable.

Hyndman and Wolkin (1942) confirmed the observation of Goetz and Marr. Nevertheless, Goetz felt that caudal extension of the sympathectomy would ensure complete sympathectomy of the upper extremity. Thus, initially, the third

thoracic ganglion and intervening trunk was removed or cauterised in addition to the second ganglion and, later, the operation was extended to include the fourth thoracic ganglion.

No difficulty is encountered in removing the sympathetic chain from the second to the fourth thoracic ganglion through the anterior approach. However, the sympathetic could be removed quite easily approaching the chain from the axilla. The axillary approach is better because, apart from hiding the scar, the chain could be removed without opening the pleura, which could be stripped quite easily.

Finally, complete revision of the method of sympathectomising the upper extremity has occurred in the past twelve months. de Takats' (1940) view and experience that extending the sympathectomy cranially resulted in lasting sympathectomy for Raynaud's Phenomena, is supported by the observation of the case of causalgia who has remained completely sympathectomised for thirty years. Thus, the method of sympathectomy at present used at Groote Schuur Hospital and evolved by Goetz (1948), is removal of the stellate ganglion with extension caudally to below the third thoracic ganglion and extension cranially to include the middle cervical ganglion. The operation is performed via Telford's approach anteriorly. The skin incision is about one inch above the clavicle. Although the operative field is surrounded by large vessels, with care little difficulty is encountered in this approach.

All patients develop a Horner's Syndrome on the side of operation. This is maximal for the first eight days after operation but a considerable improvement takes place thereabouts and little difference is observed on the two sides. Where the operation is performed bilaterally there is no

/apparent

apparent difference. It is of interest that in those cases where the middle cervical ganglion is removed the Horner's Syndrome appears less than in those patients where the stellate ganglion only is resected.

It is still too early to assess the results of this procedure for Raynaud's Phenomena.

/III. RAYNAUD'S PHENOMENA.

III RAYNAUD'S PHENOMENA

(a) AN HISTORICAL REVIEW

Ever since Maurice Raynaud described, in 1862, the vasospastic changes in the extremities which may go on to gangrene, a difference of opinion has existed as to what constitutes "Raynaud's Disease". Raynaud himself, in describing the condition which was later to bear his name, said: ".....that there exists a variety of dry gangrene affecting the extremities which it is impossible to explain by a vascular obliteration - a variety characterised especially by a remarkable tendency to symmetry, so that it always affects similar parts, the two upper or lower limbs, or the four at the same time; further, in certain cases the nose and the ears; and I hope to prove that this kind of gangrene has its cause in a vice of innervation of the capillary vessels....."

Raynaud was not the first to describe the condition, for he himself quotes several authors as having recognised the entity. Thus Rognetta (quoted by Raynaud) in 1834 reported a case of so-called spontaneous gangrene of the extremities associated with colour changes. In 1842 Huguier (quoted by Raynaud - p.45) reported the case of a boy of seven-and-a-half years who had "spontaneous gangrene". Virchow (quoted by Raynaud - p.6) recoghised that gangrene might occur in the absence of thrombosis.

Racle in 1859 observed the constant limitation of the gangrene to the skin and also the maintenance of well-being, so frequently a part of the condition. However, probably the first known case of Raynaud's Phenomena was observed in 1629 and was described by Bernard Schroeder as a symmetric, recurring form of gangrene of the extremities in a young girl:

/Raynaud

Raynaud in his original thesis commented on the colour changes in the digits on exposure to cold and noted that the gangrene is mostly limited to the skin, or, to a very small extent, beyond. He noted that, in its simplest form, the local syncope is a condition perfectly compatible with health. "It is the phenomenon known under the name of the 'Dead Finger'."

The minimal requirements for diagnosis as laid down by Raynaud were:-

1. The intermittent attacks of discolouration of the extremities.
2. Absence of evidence of organic arterial occlusion.
3. Symmetric or bilateral distribution.
4. Trophic changes, when present, limited to the skin, and never consisting of gross gangrene.

Apart from these criteria many cases were labelled as "Raynaud's Malady" because of the development of symmetrical gangrene. Such "symmetrical gangrene" may occur during the course of acute infections such as Typhoid and Typhus or during convalescence from Pneumonia. These cases are often recorded as examples of Raynaud's Disease.

The cases associated with acute infections could not be included as cases of Raynaud's Disease. This prompted Hutchinson (1896) to observe that all those conditions grouped together under Raynaud's Malady should be properly classified. Raynaud himself included the case displaying many attacks of discolouration and the case displaying a single attack of symmetrical gangrene in one pathogenic category. He believed both types to be the result of spasm of the vessel wall.

Lewis and Pickering (1934) considered that the term "Raynaud's Disease" should be abandoned. Instead the term "Raynaud's Phenomena" should be used to signify "the active and intermittent closure of the small arteries of the

/order

order of those supplying the digits, a closure manifesting itself clinically in a pallid or fully cyanotic state of the affected skin."

Lewis and Pickering realised, however, that Raynaud's Phenomena could not be regarded as the result of one set of circumstances. Thus it could be purely aspasmodic affair but it could be superposed, quite easily, on those cases with obstructive lesions of the digital vessels or even more proximal vessels. In the latter type of case, the arterial supply may be encroached on by either thrombotic or embolic processes. The anastomotic channels may be poorly developed and subsequent normal increases of tone, such as are induced by cold, will cause transient arrest or conspicuous reduction of blood-flow. Thus the original disturbance may be a sudden and non-recurring event; but a proneness to attacks of cyanosis remains which is wrongly regarded as signifying active disease.

Adson and Brown (1929) had classified patients clinically into four groups:-

1. So-called normal persons, predominantly female, who have cold hands and feet and frequently suffer mild degrees of pallor in symmetric single digits - the so-called "dead finger" usually associated with moist, clammy, cold extremities. They are frequently of asthenic type and suffer easily from cold. These subjects have been classified by Mueller (1913) as having a vasomotor constitution.

2. Persons in whom the disturbances in colour in the extremities are more profound, frequently paroxysmal in nature with lowered temperature.

3. The aggravation of the trouble is more. The attacks of pallor are more intense, more painful

/and recovery

and recovery more difficult. The changes are induced by the least changes in temperature. The hands become swollen and puffy and minute areas of gangrene occur in the tips of the fingers, with symmetric distribution.

4. More severe but rarer type in which gangrene may develop in the entire end of the symmetric digits without prolonged intercedent history of vasomotor disturbance.

All these groups fulfil the criteria laid down by Raynaud; namely symmetry, intermittency or paroxysmal nature of the disturbance in accordance with its functional basis and the existence of pulsations of the arteries of the affected part.

These groups represent the same underlying fault of the vasomotor mechanism. The term Raynaud's Phenomena should be reserved for the last three of the groups according to Adson and Brown. However, the last group falls into that category mentioned above by Lewis and Pickering.

Depending on the severity of the symptoms a gradual transition is noted in which the reaction of the extremities to the exposure of cold is the determining criterion of classification. This ranges from the normal response to cold to those cases resulting in minute symmetric areas of gangrene.

Hunt, perhaps, best defines Raynaud's Phenomena as "intermittent pallor or cyanosis of the extremities precipitated by exposure to cold without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin."

In addition to the criteria laid down for diagnosis by Raynaud, Allen (1932) insists that the condition must have been present for a minimum of two years. He also stipulates

/that there

that there must be no evidence of disease to which it could be secondary. Allen and Brown (1932, 1937) comment on the fact that the absence of pain is so striking that severe pain during the attacks is exceptional and its presence militates against the diagnosis of a primary vasomotor disturbance.

(b) ETIOLOGY.

The exact cause of Raynaud's Phenomena is not known. However, numerous predisposing factors are known to play some part in the mechanism.

The onset of Raynaud's Phenomena usually occurs in the early decades of life, predominantly during the first and second decades. Should the Phenomena occur after this period it is likely that some other primary factor would be found responsible.

Heredity may play some part and it is not unusual to have a patient disclose, on careful questioning, that some other members of the family have suffered from cold hands or feet, "dead fingers" or other manifestations of vasospasm.

Raynaud, himself, commented on the fact that the spasm occurs in subjects who are characterised by a nervous predominance, particularly young women, hysterical people and children.

Various other authors have stressed the nervous and emotional make-up of persons with Raynaud's Phenomena. Many of them exhibit evidence of an inherent biologic inferiority and nervous instability.

The predilection of Raynaud's Phenomena for the female is one of the outstanding etiologic factors. At the Mayo Clinic the ratio of females to males is 5 : 1. (Allen,

/Barker

Barker and Hines-- 1946). Various writers have reported that the Phenomena occurs in females in from 60 to 90 percent. of cases (Allen and Brown - 1932, Smithwick - 1937). 100 percent. of the patients examined in this series were females. Further, of patients suffering from Raynaud's Phenomena, observed at Groote Schuur Hospital, females constituted 80 percent.

Allen and Brown (1932) comment on this predilection for females and they suggested this large incidence makes its diagnosis in the male at best tentative. In their experience, in cases where a diagnosis of Raynaud's Phenomena in the male has been made early, subsequent follow-ups of these patients show that evidence of organic occlusion of the peripheral arteries usually has been found.

Lewis and Pickering (1934) in classifying their cases of Raynaud's Phenomena seem to indicate that there are two main groups. The first group includes:-

i. Raynaud's Phenomena, i.e. intermittent spasm of digital arteries, without complications.

ii. Raynaud's Phenomena with local nutritional changes.

In the second group are included the following conditions associated with Raynaud's Phenomena:-

i. Generalised Scleroderma: Goetz and Cole-Rous (1942) have pointed out that Raynaud himself was well aware of the association of scleroderma and Raynaud's Phenomena. Goetz and Cole-Rous have demonstrated other lesions, viz. calcinosis, oesophageal spasm and duodenal ileus, associated with Raynaud's Phenomena. The combination of Raynaud's Phenomena with the described visceral changes was stressed by the authors. In a later paper Goetz (1945) classified these cases as progressive systemic sclerosis.

/In their

In their cases Raynaud's Phenomena preceded the visceral changes by many years.

ii. Raynaud's Phenomena arising out of local injury. This includes the use of vibrating tools, e.g. pneumatic drills. During the past two years one case of Raynaud's Phenomena in a male was associated with his employment as a crane-driver.

iii. Raynaud's Phenomena may be associated with paroxysmal haemoglobinuria on exposure to cold. It has even been proposed that cold haemagglutination, with which the cases of paroxysmal haemoglobinuria are associated, may be the cause of the ischaemia in a large number of cases of Raynaud's Phenomena (Iwai and Nin - 1926, Legoff - 1933). However, Stats and Wasserman (1943) investigated four cases of Raynaud's Phenomena and did not find any evidence of cold haemagglutination.

iv. Lewis and Pickering (1934) has observed that Raynaud's Phenomena were often superimposed on organic change in the vessels of the extremity. These changes occurred in elderly subjects and were found to be on an arteriosclerotic basis.

v. In reviewing two hundred cases of Thrombo-angiitis Obliterans Allen and Brown (1928) found that Raynaud's Phenomena were the first symptoms in 12 percent. and that it occurred at some time during the course of the disease in 30 percent. However, the classical three-colour phase in Raynaud's Phenomena occurred in only 27 percent. (Hines and Christensen - 1945). Like other subjects with Raynaud's Phenomena the exciting mechanism was cold in every case. They found, too, that functional or neurotic disturbances were common.

/vi. Syphilis

vi. Syphilis has been held to be the causative factor of Raynaud's Phenomena. Thus Semon (1913) and Weber (1913) both comment on the association of chronic Raynaud's Phenomena and Syphilis in cases described by them.

vii. Endrocrine disturbances have been associated with Raynaud's Phenomena. Kleinefelter (1936) reported on a woman of thirty-four with paroxysmal attacks of Raynaud's Phenomena associated with the menses. In this case treatment with oestrogenic substance resulted in complete cure. In some cases attacks of Raynaud's Phenomena are aggravated at the time of menstruation. Also some cases occur in which Raynaud's Phenomena completely ceased during pregnancy.

Although none of the patients included in the present series had either symptoms or signs suggestive of any hormone disturbance, several patients seen at the Groote Schuur Hospital were treated by the implantation of ovarian extract. No ill effects resulted but no difference was observed in the number or duration of the attacks.

Pribram (1920) described a patient with Raynaud's Phenomena during the menopause. The sella turcica was noted to be deepened and widened. Injection of pituitary extract led to the disappearance of the Raynaud's Phenomena.

Peet and Kahn (1936) describe a case of Raynaud's Phenomena occurring in a patient with a tumour of the hypothalamus. The attacks of cyanosis and coldness appeared several hours before death.

Cold extremities are not uncommon in myxoedema. Myxoedematous patients may actually present with Raynaud's Phenomena. A case occurred recently at Groote Schuur Hospital where sympathectomy had been carried out on one side for Raynaud's Phenomena. Subsequent follow-up of the patient revealed the true nature of the complaint. Administration of thyroid cured the "Raynaud's Phenomena".

/viii. Arthritis

viii. Arthritis may be associated with vasomotor phenomena.

One patient at Groote Schuur Hospital had had sympathectomy performed for Raynaud's Phenomena of the hands. On the fourth post-operative day Raynaud's Phenomena recurred. No difference was apparent between the pre- and post-operative attacks. Subsequent follow-ups showed that the Raynaud's Phenomena were secondary to Rheumatoid Arthritis.

ix. Cervical ribs may cause Raynaud's Phenomena.

Removal of the offending rib results in complete cure.

Crutch pressure in the axilla may give rise to Raynaud's Phenomena of the upper extremities.

x. Goetz (1947) has observed that a high percentage of patients develop Raynaud's Phenomena of the hands following the "Smithwick Operation" for Hypertension. This occurs particularly in those patients with a high vasomotor tone, which, being counteracted by the high blood pressure, does not manifest itself as Raynaud's Phenomena before the operation. Once the systemic blood pressure has been lowered by sympathectomy, the original high vasomotor tone may produce Raynaud's Phenomena. The fact that this does not occur in the lower (sympathectomised) extremities is regarded as evidence that this high vasomotor tone is neurogenic and not humoral in nature. (Goetz - 1947).

It is interesting to observe that at Groote Schuur Hospital Cole-Rous has extended the "Smithwick Operation" so that the second thoracic ganglion is included in the sympathetic tissue removed. In these cases Raynaud's Phenomena does not occur.

xi. Among such irritant phenomena Bennett and Boulton (1928) describe a case of Raynaud's Phenomena occurring in a patient who died of Carcinoma of the stomach. Autopsy examination of the right inferior cervical ganglion

/revealed

revealed carcinomatous metastases infiltrating normal sympathetic ganglion cells.

Peet and Kahn (1936) describe a case of Raynaud's Phenomena of the feet where on microscopic examination there was marked leucocytic infiltration and increase in stroma in the lumbar sympathetic ganglia.

It has not been unusual to find, in cases of Thromboangiitis Obliterans or Raynaud's Phenomena of the lower extremities, that difficulties have arisen in dissecting out the lumbar sympathetic trunk. Numerous glands are found in many cases and the chain may actually be buried in a mass of inflammatory connective tissue.

In those cases of Raynaud's Phenomena in the present series where transthoracic sympathectomy had been performed, it was the rule to find adhesions present at the apices. The difficulties of the transthpracic thoracoscope have to a large extent been due to the numerous adhesions found.

What part these inflammatory lesions play in the production of Raynaud's Phenomena is not really known. Craig and Kernohan (1933) also have observed indications of inflammatory reaction in both the posterior mediastinum and postperitoneal tissues. However, histological observations on the ganglia removed in these subjects and normal ganglia failed to explain the vascular disturbances. All the changes were within normal limits and most of them, according to the authors, could be explained on a basis of advancing age. They further state that the noxious agent causing the vascular diseases, for which operative relief had been instituted, does not act on the sympathetic ganglia removed.

xii. Kraetzer (1935) found arsenic in the urine of seven patients affected with Raynaud's Phenomena. He treated these cases with intravenous sodium thiosulphite and the symptoms either disappeared entirely or were greatly improved.

/The association

The association of cold extremities and various nerve lesions is well known. Raynaud's Phenomena have been described in various lesions of the spinal cord, e.g. tabes dorsalis, syringomyelia and disseminate sclerosis. Peripheral polyneuritis may simulate Raynaud's Phenomena particularly where localised trophic lesions develop.

xiii. The one common factor in all cases of Raynaud's Phenomena is exposure to cold. All attacks are brought on by a lowered environmental temperature. Allen and Brown (1932) claim that generalised exposure of the body is more important in producing attacks than exposure of the digits only. They also observe that the degree of coldness necessary to induce a change in colour varied greatly.

Raynaud's Phenomena may be brought on by emotional and nervous upsets. Although not unusual, attacks are not as frequent as those caused by exposure to cold.

(c) SYMPTOMATOLOGY.

Classically attacks of Raynaud's Phenomena are divided into three phases:-

1. Stage of local syncope. In Raynaud's own words, "the skin of the affected parts assumes a dead white or sometimes a yellow colour; it appears completely exsanguine. The cutaneous sensibility becomes blunted, then annihilated; the fingers become like foreign bodies to the subject."

2. This is followed by a period of local asphyxia. The pallor of the extremity is replaced by a cyanotic colour. The affected part is deeply cyanosed - blue or blue-black.

3. A stage of active hyperaemia then succeeds and the fingers and toes become dry and hot.

/However

However, this three-phase colour in Raynaud's Phenomena occurs in only 27 percent. of sufferers (Hines and Christensen - 1945). The stage of local asphyxia may be absent when syncope is succeeded by active hyperaemia.

Raynaud, in his original description, noted that swelling of the fingers and toes was common.

In the cyanosed phase, Raynaud noted less livid patches. "These extend and coalesce and at the same time a vermillion colour shows itself at the margin, which gains ground little by little, chasing before it the bronzed colour which persists longest in the parts where it commenced, i.e. in the most peripheral parts. Finally, a patch of deep red is formed on the extremities of the fingers. This patch gives place to the normal pink colour and the skin has returned to normal.

"Sometimes the digits become black and entirely insensible; small phlyctenulae appear upon one digit (particularly the little finger), fills with seropurulent fluid and ulcerates."

These phenomena may appear on other digits or remain confined to one digit. Where ulceration occurs a small, white, depressed cicatrix is left on the pulp of the finger. It is only the most superficial layer of the true skin that is involved. "This progress of the malady is not incompatible with veritable sloughs. But that which strikes one most is the slender form the ends of the digits take, the hardness of their tissue and their shrivelled aspect."

The attack may occur in a single digit or even the terminal phalanx of a single digit may be involved. However, the lesion is most commonly symmetrical and involves more than one digit. Mostly those digits on the ulnar side are involved. The hand or wrist may undergo the same changes

/as the fingers

as the fingers and Raynaud has described a case where cyanosis extended up to the insertion of the deltoids. However, the peripheral distribution is the most common. During the attack the radial artery is usually easily palpable.

Attacks occur most often in the upper extremities. Occasionally, one hand suffers more than the other. Frequently all four extremities are equally involved. At times the feet show marked vascular spasm while the hands show little. Allen and Brown (1932)observed that in 47 percent. of cases both feet and both hands were involved whereas in a further 47 percent. the hands only suffered.

The edges of the ears, the tips of the nose, the chin, the lips and the eyelids have all been described as suffering from Raynaud's Phenomena in various cases.

Mental depression accompanies some attacks of Raynaud's Phenomena. One case in the present series had both auditory and visual hallucinations during a severe attack in the hands. These lasted for two or three days before clearing up. A competent psychiatrist considered that the hallucinations could be described as "Cerebral Raynaud's Phenomena." Mental symptoms are more common in those cases associated with Progressive Systemic Sclerosis. In the latter type of patient, as well as in the sufferer of uncomplicated Raynaud's Phenomena, anorexia and vomiting may precede or accompany an attack.

Osler reported a case complicated by three attacks of aphasia, with hemiplegia, ending in complete recovery. Deafness, tinnitus, taste disturbances and disturbances of vision have all been associated with Raynaud's Phenomena. Raynaud, himself, reported a case where vision became blurred and confused in the period following an attack. He observed the retinal artery in this case and noted that spasmodic contraction of the artery could actually be seen. Anderson and Gray (1937) and Carpenter and Carpenter (1938) have observed

/the contractions

the contractions of the retinal artery and its branches and noted that the arteries appeared as white streaks whilst three secondary veins contained segments of blood.

All cases of Raynaud's Phenomena in this series were examined ophthalmoscopically. No gross lesions were demonstrable in any case. At the time of examination certainly neither spasm nor segmentation was a feature.

The duration of the attack of Raynaud's Phenomena varies considerably. The fingers may be white and numb for a few minutes, such as during bathing in cold water, and may rapidly return to normal on exposure to a warmer temperature. The attack may last for hours and during the cold winter months the digital vessels may actually be in a state of continual spasm.

From beginning in a uniform manner the condition usually progresses steadily with periods of discolouration of the digits and intervening periods of entire normality. The condition may improve temporarily or remain stationary. At times progression takes place with surprising rapidity. Spontaneous cure is very rare or unheard of. (Smithwick - 1937).

In those cases where progression has occurred, the fingers assume the characteristic shape described by Raynaud. The pulps of the fingers atrophy and the fingers taper to the tips. The skin overlying becomes thickened and inelastic. Radiologically the terminal phalanx shows atrophy with disappearance of the ungual tuft. (de Lorimer - 1943).

Scars of previous ulceration are present. Calcinosis also may be manifest. With the loss of elasticity of the skin, joint movements are interfered with.

The skin appendages atrophy. Cessation of growth of the nails occurs and the nails may actually drop off. With all these manifestations of relative ischaemia due to the continuous spasm, secondary infection is common and very

prone to occur. This may lead to even more extensive gangrene than the superficial destruction observed in the earlier attacks.

These crippling effects of the Phenomena, however, take place over a period of time. Allen and Brown (1932) observe that the lesions take over fifteen years to develop.

(d) PATHOLOGY.

Raynaud observed from the start that the main vessels to the extremity were patent. He did not believe that an actual arteritis was the responsible factor. He commented on the fact that although stuctural lesions of the vessels may be accessory factors, he was unable to find in these lesions an adequate cause to account for the gangrene. He suggested that gangrene was secondary to persistence of capillary spasm.

The attack commences as a capillary spasm whereby the blood is driven forward and the extremity becomes pale and insensible. This is responsible for the stage of local syncope. He also commented that, during this period, the venules as well as the arterioles were in spasm.

In that phase termed "local asphyxia" the condition is more advanced. After an initial period of capillary spasm, there occurs a period of reaction, but it is an incomplete reaction. The vessels with the fewest contractile elements, viz. the venules, return to their initial calibre or even beyond. At this stage the arterioles are still closed and venous blood flows back into the finest tributaries. The extremities thus take on that hue which is indicative of venous blood in the capillary network.

Should, however, the nature of the capillary spasm be so intense and last longer, anoxia results in damage to the capillary wall, with resulting exudation into the superficial tissues. Ulceration and gangrene may then occur.

/Raynaud's

Raynaud's opinion was that the Phenomena were due to a vasomotor neurosis. Thus "to sum up in a more definite from I would say that in the present state of our knowledge, local asphyxia of the extremities ought to be considered as a neurosis characterised by enormous exaggeration of the excito-motor energy of the grey parts of the spinal cord which control the vasomotor innervation."

Raynaud's contention that the primary source of the condition was derangement of the nervous system has been supported by various observers. Thus Simpson, Brown and Adson (1930) and Adson and Brown (1929) were of the opinion that in Raynaud's Phenomena the abnormality during the early stages is wholly in the vasomotor nerves. Spurling, Gersman and Rogers (1932) concurred. Villaret and his co-workers (1935), too, were convinced that the paroxysms of Raynaud's Phenomena were entirely mediated by the sympathetic nervous system.

Mufson (1944) after several years' observation felt that in Raynaud's Phenomena a continuous flow of vasoconstrictor stimuli is maintained by a chronic psychosomatic disturbance. These induce a partial angiospasm which then becomes complete when the skin is exposed to cold.

Sir Thomas Lewis (1929) observed that "in the several cases paralysis of the vasoconstrictor nerves does not prevent the vessels of the fingers from being subsequently thrown into a complete obstructive spasm by local application of cold. Also if the vessels were already all spontaneously in a state of full spasm when the vasomotor paralysis takes effect, the paralysis does not greatly relieve this spasm; it produces only a little relaxation of the vessels from their complete closure."

/Thus, according

Thus, according to Lewis the tone of the vessels of the finger, when in spasm, is simultaneously maintained from two sources, namely by the exaggerated effect of temperature acting locally and by the normal vasoconstrictor tone. It is because it is only a normal vasoconstrictor tone that is abolished that the spasm fails to disappear, though slightly lessened in degree.

The primary cause of spasm of the digital vessels in Raynaud's Phenomena is not an abnormal vasomotor impulse but a local fault of the vessels. Local applications of heat and cold show that the spasm is profoundly influenced by temperature, in response to which the vessels behave abnormally. The abnormal reaction to cold is a direct one and is developed from a peculiar condition of the vessel wall locally.

Subsequent investigations by Lewis and his co-workers seem to support this contention. Thus Lewis and Landis (1931) repeat the assertion that the fault is a local one with susceptibility to cold producing a state of spasm. Lewis and Pickering (1934) agree that the local fault is still unknown. They observed that, although intimal changes may be present in the group of severer cases, it is impossible to say that this is the primary pathological change or whether it is secondary to the longstanding and severe spasm. The intimal thickening plays but a subsidiary part and the local fault in the vessel wall is regarded as a functional one.

The concept of Lewis, that the primary fault lies in the vessel wall and that, although vasonconstrictor tone may be superadded, it is not the responsible factor, has been supported by numerous observers. Thus Craig and Horton (1938) also maintain that the central vasoconstrictor effect does play an important part in the pathogenesis of Raynaud's

/Phenomena

Phenomena but that the presence of both central and local factors must be considered.

Heinbecker and Bishop (1938) do not subscribe to the view that Raynaud's Phenomena is the result of sympathetic hyperfunction. In fact, they point out that conditions in which hyperfunction does exist are not associated with Raynaud's Phenomena. The fact that the paroxysm may be initiated by emotional excitement as well as by exposure to cold is easily explained by considering that the mechanism of constriction is a combined reflex and humoral one. Cold produces a reflex excitation of vasoconstrictor impulses to the blood vessels and also reflexly produces an increased secretion of epinephrine. They believe that reflex activity of the autonomic nervous system is a definite factor in the development of an attack. In normal persons, on exposure to cold, there is a reflex constriction of blood vessels. They do not believe that this reflex response in persons with spastic vascular disease is any different from that in a normal person but that there is a definite quantitative increase in the response. The cause, in their opinion, is to be regarded as a constitutional change in the walls of the blood vessels. They say that cold itself plays a minor role as a direct constrictor agent in the typical spasm. It is merely the stimulus.

Heinbecker (1940) and Hyndman and Wolkin (1942) consider that the condition is primarily a vascular and not a sympathetic disorder.

Stats and Wasserman (1943) have postulated the hypothesis of cold haemagglutination as a cause of the Raynaud's Phenomena. Lewis (1941) has emphasised that on exposure to cold vasoconstriction of the peripheral blood vessels and a fall in skin temperature is a normal feature.

/The blood

The blood flow to the relevant areas is reduced. If, at the same time, marked haemagglutination occurs within these narrowed areas, or in the capillaries of the regions, further retardation or even cessation of blood flow might occur. In a very short time the colour and sensory changes of Raynaud's Phenomena supervene with warming of the body. Vasodilatation and disruption of the haemagglutination would be followed by a return of blood flow. Such a process could occur repeatedly on exposure to cold. Corroborative evidence, however, has not been forthcoming, in spite of the known association in some cases of Raynaud's Phenomena and paroxysmal haemoglobinuria on exposure to cold.

White (1936) has commented that a lasting vasodilatation can only be obtained when adrenal secretion is abolished. Evidence that Raynaud's Phenomena may be associated with disturbance of the humoral mechanism of the peripheral vascular control, has been suggested by Johnson (1941). The fact that Raynaud's Phenomena has occured after the administration of pilocarpine may add weight to this theory. However, there is not conclusive proof of any definite humoral factor being responsible for Raynaud's Phenomena.

Sympathectomy is the treatment recommended at Groote Schurr Hospital, although Lewis' concept that the prime factor in Raynaud's Phenomena is an inherent fault in the vessel wall, is supported by the results obtained following such operation. Various types of sympathectomy have been performed but the final outcome is that subjectively the condition is improved but after a period the attacks recur, in the majority of cases less severely than before operation.

The inherent sensitivity of the vessel wall on exposure to cold is not affected by sympathectomy. Vasoconstriction on exposure to cold will still occur but <u>reflex</u> vasoconstriction will not occur after sympathectomy. Sympathectomy thus removes all the reflex causes of vaso-

/constriction

constriction without interfering with the local responses of the vessel wall.

Numerous observations have been made on the changes occurring in the vessels during an attack of Raynaud's Phenomena and on other occasions. Knowledge of the pathologic state of the digital arteries in the early stages is practically nil. In the advanced stages intimal thickening and other changes are usually present. These changes, however, are the result of the vasospasm rather than the cause of Raynaud's Phenomena.

Lewis (1938) has shown that, in warm-handed adults, the digital arteries usually show distinct intimal thickening as age increases. In those cases of intermittent spasm of the digital arteries, exemplified by the mildest form of Raynaud's Phenomena, there is no more intimal thickening than is found in the arteries of warm-handed subjects of similar age.

Similarly, the cases of greater severity may show more intimal thickening but it was no more than that found in many subjects who present no symptoms. Thus attacks of discoloured fingers in these cases must be ascribed to over-action of the muscular wall.

In cases of thrombo-angiitis obliterans and progressive systemic sclerosis presenting Raynaud's Phenomena, there is a conspicuous evidence of occluding disease of the digital arteries. In these cases, however, Raynaud's Phenomena occur as the result of exposure to cold in an extremity with a blood supply already interfered with.

The vessels at fault in Raynaud's Phenomena appear to be the digital arteries (Lewis - 1931). The main vessels of the extremities are patent and pulsations are present in the usually palpable arteries. Allen (1946) employed arteriography and found that the digital arteries of most sufferers

/of Raynaud's

of Raynaud's Phenomena do not appear to be filled normally - there was absence of filling of the distal part of the digital arteries and diminished calibre of these. But similar changes were seen in asthenic persons who did not have Raynaud's Phenomena.

Brown (1925) observed that the stage of pallor indicated complete constriction of the terminal arterioles, capillaries and small venules. The blood ceases to flow through the capillaries which are visible because of the small segments of static blood retained in them. The degree of constriction and amount of blood in the exposed capillaries and small venules determine the visible colour reaction.

Numerous observations on the capillaries in Raynaud's Phenomena have been made. It fact, Deutsch et al (1941) claim that capillaroscopy will reveal abnormal capillaries even before the appearance of clinical symptoms. They further suggest that the severity of the disease could be defined more accurately by capillaroscopy than by the gross clinical findings.

Roth (1938), in discussing the capillaries of the nail folds in Raynaud's Phenomena and Scleroderma observed that the capillaries vary according to the phase of the attack. Thus in the stage of syncope the capillaries are contracted. As Adson and Brown (1929) observe, few capillaries are visible, the filling of the loops with blood is incomplete and the capillaries have a segmented or broken appearance. The contained blood in the capillaries is static and blood is not observed entering the capillary loops from the arterioles. The collecting venules are usually invisible or contain small amounts of blood.

In the stage of cyanosis blood is admitted to the capillaries both from the arterioles and by retrograde

/flow

flow from the venules. (Adson and Brown - 1929, Roth - 1938). The capillaries become dilated, and an increased number becomes visible. The flow in the capillary loops is stationary or occurs only after long intermissions. There is gradual deoxygenation of the capillary blood with increasing cyanosis. The capillaries may become greatly distended and may lose their characteristic shape. The collecting venules become dilated.

After a variable period the capillary flow is suddenly resumed as a result of complete relaxation of the arterioles. The flow of blood in the capillary loops become rapid and the blood changes to a bright red colour. Many additional capillaries open so that the stage of rubor is over-recovery. Both capillaries and venules remain dilated and the venules may contain red oxygenated blood.

The cyanosis is not caused by an obstruction on the venous side. (Lewis - 1931). Landis (1931) also observed that the stasis in Raynaud's Phenomena is not due to venous obstruction. The spasm is apparently on the arterial side and not the venous side of the capillary network.

Although little is known of the changes occurring in the vessels during the early stages, numerous observations on the vessels in the later stages show gross changes. In those cases of Raynaud's Phenomena which go on to sclerodactyly or are associated with progressive systemic sclerosis gross changes occur in the intima. In citing a case of the latter, Goetz (1945) comments on a marked proliferation of the intima undergoing "fibrinoid" degeneration. Fragmentation of the internal elastic membrane and infiltration of round cells occur with plasma cells grouped around the small vessels. The pathology of these cases of Raynaud's Phenomena, secondary to some factor or associated with visceral lesions as in

/progressive

progressive systemic sclerosis does not explain the true nature of the lesion.

(e) DIAGNOSIS.

The diagnosis of Raynaud's Phenomena may prove difficult. One of the cases in the series was treated for years for "anaemia" before the true nature of the condition was realised. In the majority of patients, however, the history of attacks ensuing on exposure to cold clinches the diagnosis.

In all cases a primary cause must be diligently sought. Thus numerous investigations - chemical, radiological, etcetera must be carried out.

(f) TREATMENT.

The treatment of Raynaud's Phenomena is not satisfactory. In those cases where a primary factor is responsible for the lesion, removal of this factor will result in a cure of Raynaud's Phenomena. However, this is the exception rather than the rule.

Measures to improve the general health and to protect the patient from worry, emotional disturbances, and over-fatigue should be used. Attention to clothing and the choice of a suitable climate should be considered. Exposure to cold should be reduced to a minimum.

Numerous drugs have been tried. Thyroid extract, calcium lactate, nicotinamide, ovarian extract, etcetera have been tried and have proved useful on occasions. Acetylcholine by injection, the administration

/of intravenous

of intravenous T.A.B. vaccine have been used at one time or another to produce a lasting vasodilation.

However, as Smithwick (1937) points out, medical treatment is not satisfactory and no drugs have been found that effectively inhibit vasoconstriction.

It is generally agreed that sympathectomy is the treatment of choice. The operative results are most striking when done early in the condition before marked local changes have taken place. However, even in the advanced cases, the abolition of colour changes and the anhidrosis produced make the result worthwhile even though there be only a slight elevation of skin temperature. (Smithwick - 1937).

(g) THE EFFECT OF SYMPATHECTOMY.

The immediate effect of sympathectomy of the upper extremity in Raynaud's Phenomena is a dry, warm extremity. With the vasodilatation that takes place no attacks of Raynaud's Phenomena occur. The extremity does not sweat. From a previously cold and sometimes clammy extremity of a bluish hue, a change occurs in that cyanosis disappears, and a pink colour results.

The change in the extremity is apparent within the first twenty-four hours after operation. However, this maximal dilatation lasts about eight days when the initial complete vasodilatation begins to wear off. The extremity, however, still remains warm as compared with the normally innervated opposite limb.

"Immediately after sympathetic denervation, of whatever nature, there is always an improvement in the condition of the fingers except where actual digital thrombosis

/or extreme

or extreme sclerodactyly exists. The high skin temperature resulting from the operation, however, is not maintained and a steady decline occurs until a level is reached which is usually several degrees above the pre-operative temperature. This decline in the skin temperature occurs in both the hands and the feet and appears even when the operation is performed for non-vascular disease. It is a normal sequence to all types of sympathectomy operation, and is presumably due to the resumption of a certain degree of tone by the blood vessels by virtue of their inherent muscular activity." (Simmons and Sheehan - 1939).

Secondary changes associated with the increased blood flow to the extremity result. Thus the nails may grow more quickly and not infrequently a definite line of demarcation can be seen corresponding to the moment of sympathectomy. Previously distorted, irregularly shaped nails become smooth, pink and normal in every way. There may be an increased growth of hair on the extremity. The extremity seemsto take on a new lease of life and all signs of infection, if present, heal rapidly and completely.

With the interruption of the sympathetic pathways, all spontaneous fluctuation in pulse and digital volume, as well as the constrictor reflexes following various stimuli, are no longer obtained. Thus cooling or pinching the body (Capps - 1936) will not produce vasoconstriction in the sympathectomised extremity. Storup, Bolton and Carmichael (1935) observed the same absence of vasoconstriction with pain, fright or anger, which usually result in vasoconstriction. Lewis and Pickering (1931) observed that heating of the body will not produce vasodilatation. Johnson, Scupham and Gilbert (1933) could not produce vasodilatation by typhoid vaccine. Gellhorn and Steck (1939) found that inhalation of carbon

/dioxide

dioxide, which normally produces a marked central vasoconstriction of peripheral vessels, is abolished in the completely sympathectomised extremity.

Goetz (1946) has confirmed by plethysmography the absence of these reflex stimuli following sympathectomy. He further states that failure to evoke these responses may be accepted as evidence of the interruption of the sympathetic reflex arc.

Following sympathectomy the tone of the peripheral vessels is mainly determined by three factors:- (1) the local metabolic requirements of the tissues (effect of metabolites); (2) the local stimuli reaching the vessel wall directly from the outside, without the mediation of the nervous system (cold, etc.) and (3) the effect of endogenous substances - acetylcholine, epinephrine, etc.- reaching the vessel from the blood stream (Goetz - 1946). Therefore, as Goetz points out, the blood flow of the sympathectomised extremity may not be the same when tested on different occasions. If such influences are depressing in nature, the blood flow tends to return to its maximum as soon as such stimuli are removed.

Lewis and Landis (1931) noted, after cervical sympathectomy, that exposure to cold produces a decrease in temperature of the normal hand more quickly than the denervated one. They observed that, after extirpation of the stellate and the second thoracic ganglia in Raynaud's Phenomena, spasm of the digital vessels may occur on exposing the extremity to cold.

This observation had been noted previously by Thomas (1926). Freeman (1935) also observed that if a completely sympathectomised limb is immersed in cold water, the blood flow drops to a low level. Inspection of his curves which are characteristic for the effect of temperature on the blood flow through the normal and through the sympathectomised limb revealed that they are of the same general shape. The chief

/differ-

difference in the two curves lay in the fact that the extremes of constriction and of dilatation were absent in the sympathectomised limb.

The response of the sympathectomised extremity to the application of local heat is shown in Figure 1. (page 67). Figure 2. (page 67) represents the sympathectomised extremity after thirty minutes body heating. The extremity was then immersed in a water bath at 45°C. The volume has increased from 0.18cc. to 0.25cc. after ten minutes' immersion.

Very little has been observed on the changes in the vessels after sympathectomy. In 1897 Cehanovic reported connective tissue cell hyperplasia and nuclear changes in the muscle cells of the tunica media of blood vessels after severance of their sympathetic innervation. von Bechteren (1908) concluded that the effect of sympathectomy on the blood vessels was an increase of elastic tissue both in the intima and media accompanied by muscle cell hyperplasia. Lapinski (1908) showed rapid atrophy of the medical muscle cells at focal points in the arteries of the rabbit's ear. In others there was a hypertrophy of these cells while many of the animals exhibited hyperplasia of the intima. Kerper and Collier (1927) made histologic studies on the vessel changes in the cat and goat after sympathectomy. In the distal portions of the denervated vascular tree, atrophy of the muscle fibres, apparent dilatation of the arterial lumen and oedematous swelling in the muscle cells were noted, similar to the changes in the circular muscles found in vessels after reduced functional excitation of disuse atrophy. These studies seem to give anatomic proof of the permanent dilator effects of sympathectomy.

Although sweating is consistently absent in sympathectomised areas, Gurney and Bunnell (1942) found that no histological changes occur in the sweat glands after denervation.

/After sympathectomy

After sympathectomy the capillaries are decreased in calibre and many new capillary loops are opened. The outlines are more clearly defined. (Adson and Brown - 1929). In some of the cases of Raynaud's Phenomena where the capillaries were greatly dilated before operation, some of the large capillaries remain dilated but in a lesser degree than before operation. The flow of blood is continuous and rapid, whereas before it was intermittent and slow (Craig and Horton - 1938). Deutsch et al (1941) observed that the width of the capillary decreased and also the capillary permeability.

In cases of vasospastic disease the oxygen saturation of the venous blood rises after sympathectomy. de Takats (1937) observed that this is direct evidence that the supply of oxygen to the tissues is increased, as the venous oxygen content reflects the oxygen content in the tissues, provided arterial oxygen saturation is normal. When the venous oxygen saturation does not rise, the clinical results are poor.

Subjectively, the improvement after sympathectomy in Raynaud's Phenomena, is marked. However, with the passage of time the experience is that gradual deterioration occurs. Usually about twelve to eighteen months after the operation the upper extremities are again cold and blue. However, the majority of patients notice that the attacks are not as severe nor do the attacks last as long. Some improvement, therefore, results even though the symptoms may recur.

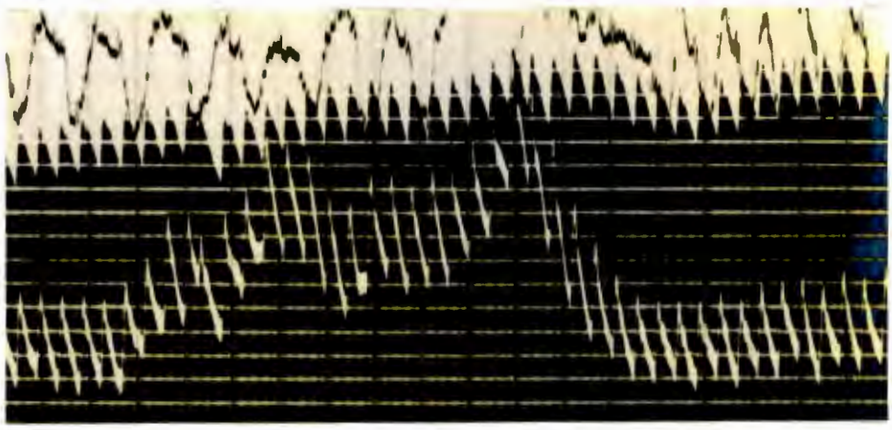


FIGURE 1.

Plethysmograph - Left middle finger (upper), Right middle finger (lower). Heat applied direct to left hand for ten minutes. Note height of pulse volume. Sympathectomy thirty years previously.

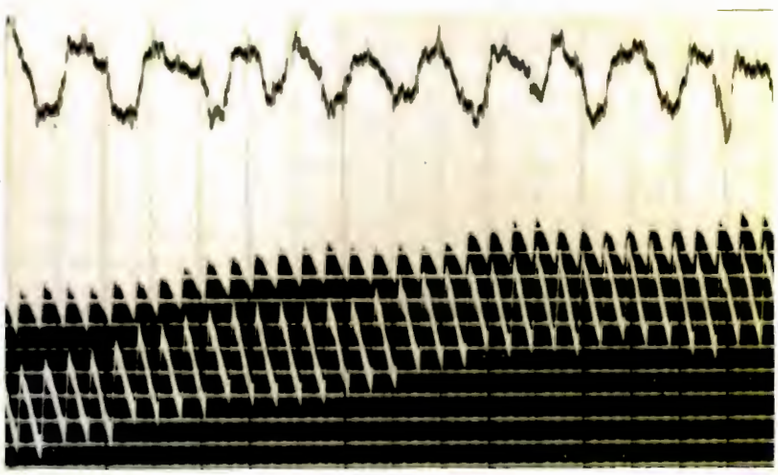


FIGURE 2.

Same case as in Figure 1 - left sympathectomy thirty years previously.

Plethysmograph - pulse volume after thirty minutes' body heating.

IV. INVESTIGATIONS OF SYMPATHECTOMISED EXTREMITIES.

(a) METHODS AND RESULTS.

In assessing the results of sympathectomy of the upper extremities in Raynaud's Phenomena, a uniform pattern was adopted. The clinical history was taken with care and stress laid on any symptom suggestive of relapse. The patients' own observations were correlated with those found on re-examination. The case histories subsequent to sympathectomy are presented in a later section. (Page 233).

Apart from the clinical assessment of the case, several special examinations had to be done. Some of these examinations and tests are standard in vascular clinics throughout the world. Plethysmography, however, is only performed at Groote Schuur Hospital.

The following special tests were performed:-

1. Sweating.
2. Skin Resistance.
3. Response to Pilocarpine.
4. Plethysmography.

Each section is reviewed and the results are then assessed as a whole as to whether the sympathetic denervation has been maintained or not.

1. Sweating.

Accompanying the vasomotor fibres to the skin are sympathetic postganglionic fibres, which, on excitation, give rise to sweating and to contraction of the smooth muscles of the hair follicles, causing erection of hair. Although sweating commonly occurs at the same time as peripheral vasodilatation as a mechanism of heat loss, it is independent of vasomotor changes. It can occur in association with vasoconstriction, as in the cold, clammy hand of fear, and it does

/not necessarily

not necessarily follow peripheral vasodilatation, viz. the hot, dry skin of fever.

Sweating may occur reflexly to increased heat (environmental or during muscular action) and to emotion. Sympathetic denervation abolishes both. However, thermo-regulatory and emotional sweating are not identical in distribution. The latter is more localised to the palmar surfaces of the hands and fingers, plantar surfaces of the feet and toes, the axillae and forehead.

Absence of sweating, induced by heat, i.e. thermo-regulatory body heating, has been generally accepted as evidence of the sympathetic denervation of a limb (Simmons and Sheehan - 1939). Such anhidrosis follows complete sympathectomy whether preganglionic or postganglionic. As Fulton (1943) points out that absence of sweating follows peripheral nerve paralysis (postganglionic section) and the line of demarcation of sudomotor and vasomotor changes follows closely the boundaries of the area of sensory loss. The sudomotor, pilomotor and vasomotor fibres are distributed by the cutaneous nerve to the same skin area as the sensory fibres. If one assumes that vasomotor and sudomotor fibres are the same or that vasomotor and sudomotor fibres have identical distributions, it is possible, by mapping out the area of anhidrosis, to demonstrate the extent of sympathectomy.

In 1928 Minor introduced his method, which utilised a colour reaction in a mixture of iodine and starch when moisture is present. This technique made possible photography of the various sites of sweating. List and Peet (1938) described the method in detail. The technique adopted in this series is essentially that of List and Peet. The mixture contains the following:-

/i. 1.52G. of

i. 1.52G. of chemically pure metallic iodine.

ii. 10cc. of Castor Oil.

iii. Sufficient Absolute Alcohol to make a total volume of 100cc.

Idiosyncrasy to iodine is excluded first in each patient.

The skin must be completely dry and clean before the mixture is applied.

The mixture is non-irritant and innocuous. The entire body, except the eyelids and the external genitalia may be painted. Initially the solution was painted on. By painting it is impossible, on occasions, to avoid transferring any possible insensible sweating from a normally innervated to a denervated area. The solution was thus sprayed on. Any suitable gas or air, under pressure, may be used - an oxygen cylinder proved most useful in this respect. In addition an evenness was obtained by spraying which is difficult to obtain by painting. Lastly, spraying is much quicker than painting.

The mixture dries very readily on the skin. The skin is left with a greasy, dark yellowish appearance.

Fine rice starch (ordinary cooking maizena proved most useful) is then dusted on. This starch powder may be dusted on with a cotton powder puff or sprayed on by oxygen under pressure. All excess is fanned or blown away. The skin so prepared has a white or ivory hue.

The patient is then covered with blankets, care being taken that none of the areas denervated are in contact with each other or with normally innervated skin. Hyndman and Wolkin (1942) have shown that sympathectomised areas will sweat if two such areas are in contact. Therefore each limb was wrapped in a clean, dry towel and towels were placed in

/the axillae.

the axillae.

Thermo-regulatory body heating was instituted by immersing both feet in water at 43 - 45°C. Heating was continued for thirty minutes, at the end of which time the blankets were removed and the patient photographed.

Sweating, whether induced by drugs or by thermo-regulatory methods, first appears as fine bluish-black dots resembling poppy seeds. As perspiration increases the fine dots enlarge gradually until they form violet-black surfaces. The areas of anhidrosis, of course, do not turn black and retain the whitish hue. The line of demarcation between a normally innervated area and the sympathectomised area, remains fairly sharp.

After the completion of the test the patient's skin can be cleansed by the application of hot water and soap.

In this series of patients thermo-regulatory body heating was the method utilised to map out the areas of anhidrosis. Sweating may be produced by pilocarpine and was observed during the completion of tests described in the section, headed "Pilocarpine" (page 148).

Results.

The patients examined by this method are classified into three groups:-

1. Raynaud's Phenomena - immediate results.

Four patients are included in this group. Sympathectomy had been carried out not longer than six months previously. In all cases the second, third and fourth thoracic ganglia were removed or cauterised.

Figure 3 (page 74) and Figure 4 (page 75) show the result of the sweating test on the twelfth post-operative

/day, after

day, after the left upper limb had been sympathectomised. There is complete absence of sweating on the whole of the left upper extremity anteriorly. Although not so obvious in the picture, sweating ceases at the midline. Posteriorly, sweating is absent to the midline and the line of demarcation extends downwards from the middle of the scapula to well below the axilla. Although sweating is not seen on the face and forehead on the sympathectomised side, it is also not present on the normally innervated side. It is impossible in this patient to state that removal of Th.2 did sympathectomise the face.

Bilateral removal of the same three ganglia was performed in the patient depicted in Figure 5.(page 76) and Figure 6. (page 77). The right side was sympathectomised four months and the left two months previously. There is practically complete absence of sweating on the whole of both upper extremities. The line of demarcation is not as sharp as in other cases. Sweating is present on the left side of the face and neck. Both shoulders are, however, completely free of sweating. Sweating is present on the posterior aspect of the upper arm as far as the elbow. This may be due to contact with normally innervated skin. The line of demarcation is sharp and extends from the same level in the midline, just at the superior border of the scapula, to the lateral border of the arm. Both axillae are sweating. Apart from the face, there appears to be a remarkable degree of symmetry in this patient. Some small deviations occur on either side but the similarity is great.

Figure 7. (page 78) depicts a patient who had had the right side sympathectomised two months previously. Sweating is completely absent on the right upper extremity

/to the midline.

to the midline. On this occasion the iodine was painted on. Subsequently spraying was the method of choice. Figure 8. (page 79) shows the sweating pattern one month later, the left side having been sympathectomised in the interim. The posterior aspect is shown. The line of demarcation is sharp and distinct. The level of anhidrosis is lower on the left side. The second, third and fourth thoracic ganglia had been removed on each side. On this occasion it was noted that some sweating was still present on the left side of the neck, face and shoulder. This was still present three months later. (Figure 9. - Page 80). No sweating was present on the right face and neck six months after sympathectomy.

In the last patient in this group sweating was absent on the left upper extremity, forehead, face and neck seven days after sympathectomy. The difference between the normally innervated and sympathectomised extremities is striking. (Figure 10. - page 81). The line of demarcation in the midline is present. Three weeks later the pattern is seen after right sympathectomy. (Figure 11. - page 82). The level on the right is lower than on the left. Figure 12. (page 83) shows the complete absence of sweating on the hands. Posteriorly, Figure 13. (page 84) sweating is absent on the neck and both shoulders. The line of demarcation is lower on the right side. The right axilla does not sweat. Sweating is present in the left axilla and on a small area on the posterior aspect of the arm adjacent to the axilla.

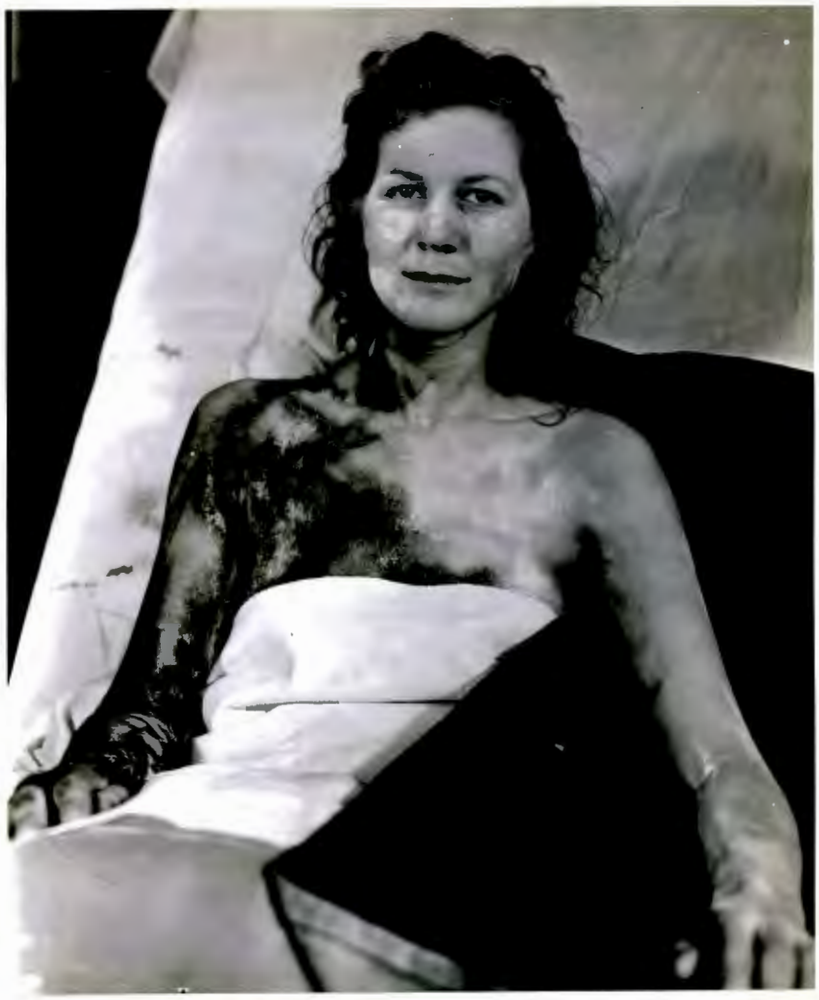


FIGURE 3.

Twelve days after removal of
Left Th.2, Th.3 and Th.4.

Anterior Aspect.

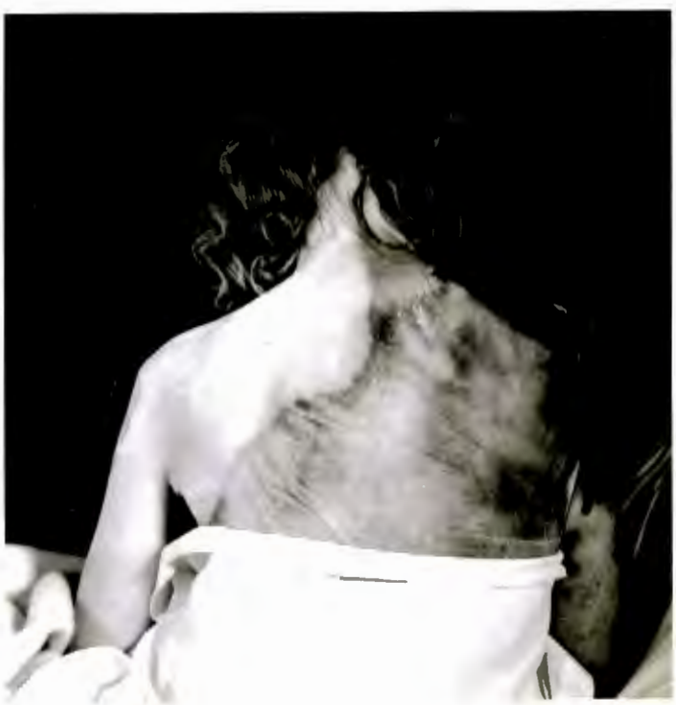


FIGURE 4.

Same case as in Figure 3.

Posterior Aspect.

FIGURE 5.

Four months after removal of Right Th.2, Th.3 and Th.4 and two months after removal of Left Th.2, Th.3 and Th.4.

Anterior Aspect

FIGURE 6.

Same case as in Figure 5.

Posterior Aspect.

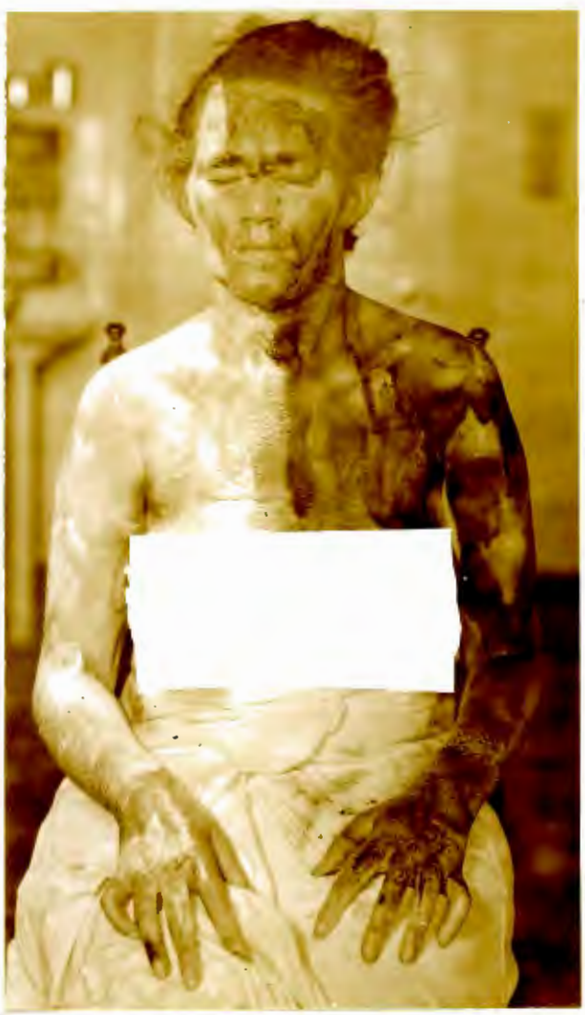


FIGURE 7.

Two months after removal of
Right Th.2, Th.3 and Th.4

Anterior Aspect

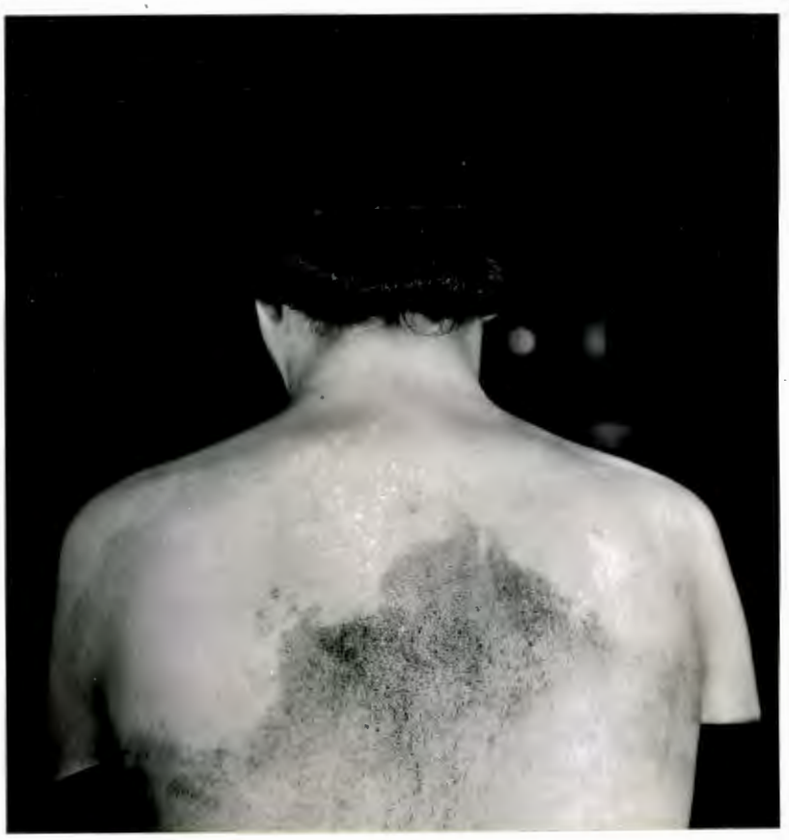


FIGURE 8.

Same case as in Figure 7.

Three months after removal of Right Th.2, Th.3 and Th.4 and One-and-a-half months after removal of Left Th.2, Th.3, and Th.4.

Posterior Aspect

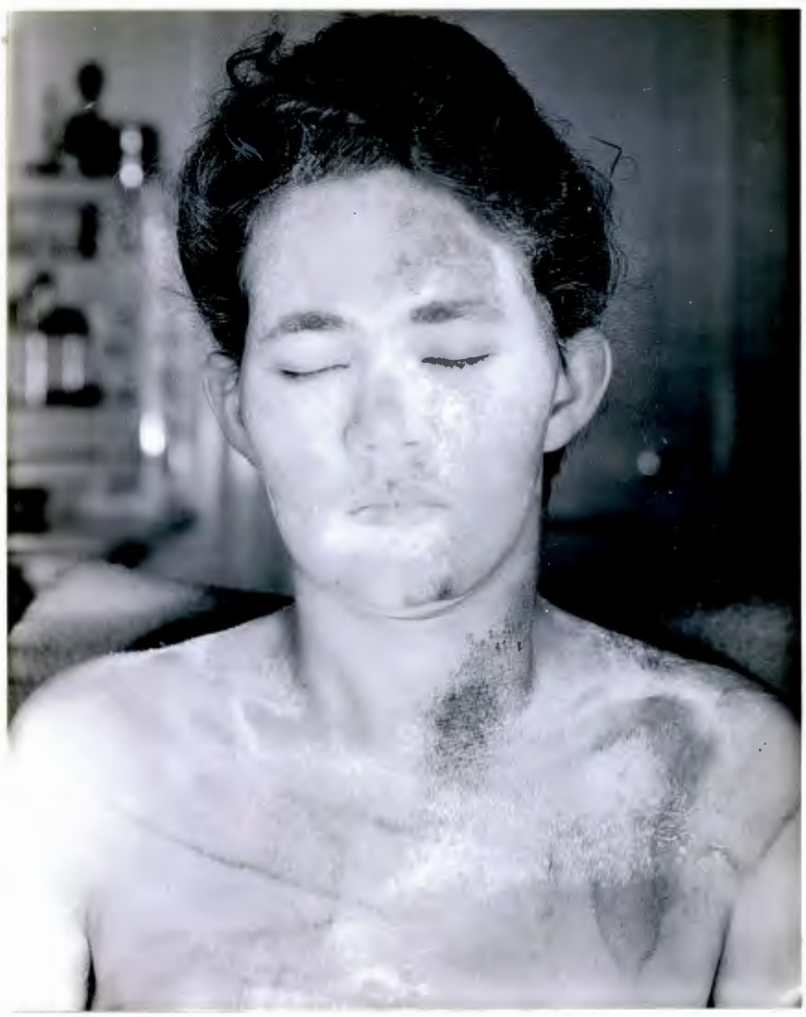


FIGURE 9.

Same case as in Figure 7.

Three months later.

Anterior Aspect.

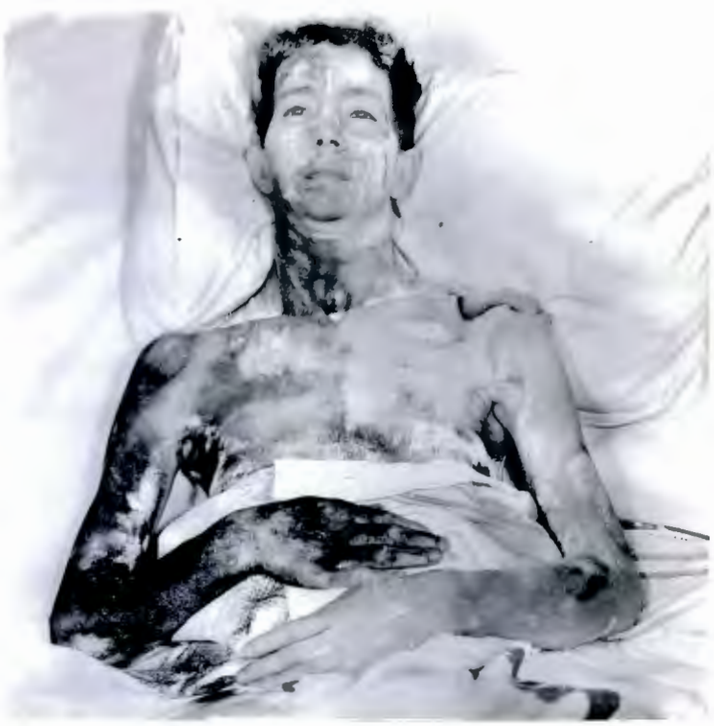


FIGURE 10.

Seven days after removal of
Left Th.2, Th.3 and Th.4.

Anterior Aspect.

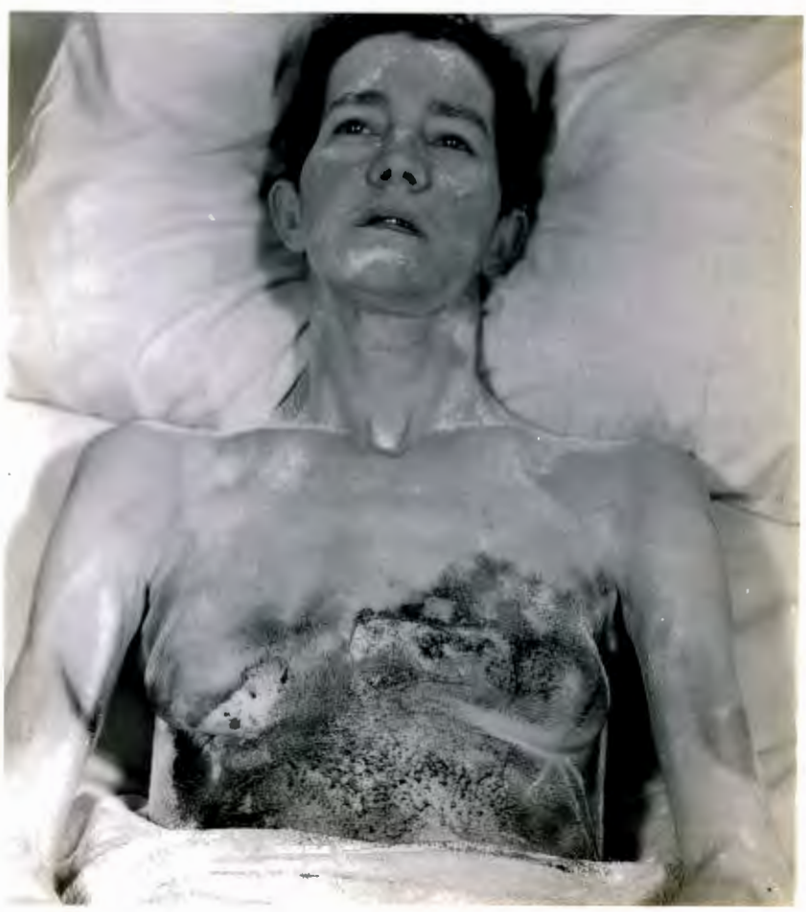


FIGURE 11.

Same case as in Figure 10.

Four weeks after removal of Left Th.2, Th.3 and Th.4.
Three weeks after removal of Right Th.2, Th.3 and Th.4.

Anterior Aspect.

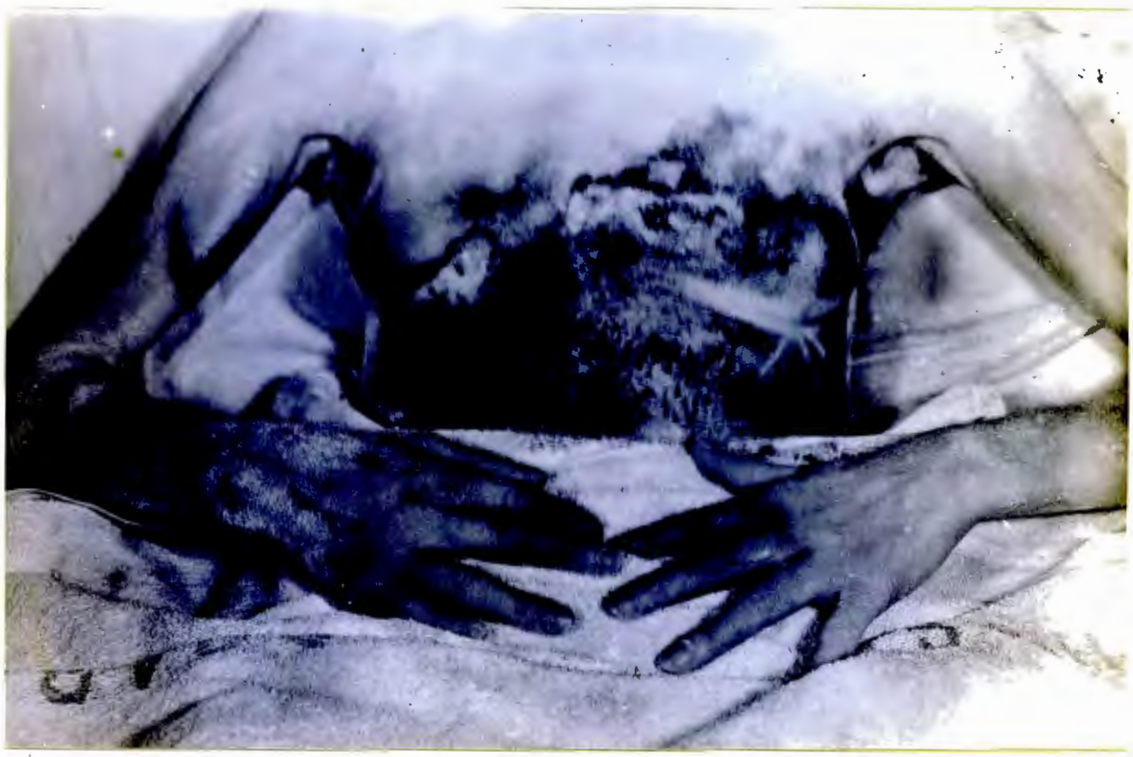


FIGURE 12.

Same case as in Figure 11.

Showing hands.

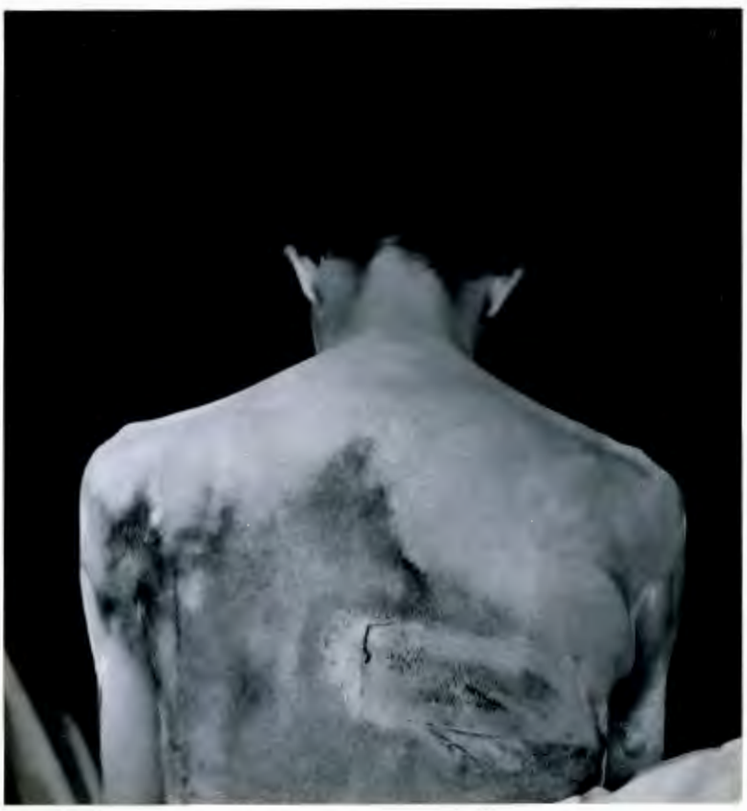


FIGURE 13.

Same case as in Figure 11.

Posterior Aspect.

Posteriorly, no line of demarcation is seen. (Figure 25. - page 98). Sweating is present fairly uniformly over the whole shoulder. No areas of anhidrosis can be defined. On the anterior aspect, too, sweating is profuse and generalised over the whole of both upper extremities. It is impossible at this stage to distinguish between sympathectomised and normally innervated skin. (Figure 26. - page 99). This is in marked contrast to the pattern obtained immediately post-operatively. (Figure 22. - page 96). Although sweating was present on both hands it was patchy in nature. Figure 27. (page 100) shows the irregularity of the pattern on the hands. On both hands the ulnar side sweats less than the other areas, although sweating appears to be least on the left thumb. The forearms, too, show an irregularity in the relatively anhidrotic areas. Sweating is relatively less on the right forearm.

extremities by removal of the second thoracic ganglia only. In this patient the second thoracic ganglion was cauterised on the right side and removed by open dissection on the left side. Sweating is present on both hands but more so on the right. Irregular patches of sweating are present on the chest and face. Three years later sweating is again present on the hands and forearms. The patchiness of the facial and thoracic pattern is still present but the areas of anhidrosis are smaller. (Figure 20. - page 94).

The second thoracic ganglion was removed on each side three years previously in the patient shown in Figure 21. (page 95). Anteriorly, sweating is present on the right hand and forearm. The left hand shows some sweating but this is considerably less than on the right. There is no gross difference in either forearm. Irregular patches of anhidrosis are present on both shoulders. Sweating is present on both sides of the neck but more so on the left. Sweating is also present on the upper lip and on the forehead.

Bilateral cauterisation of the second thoracic ganglion had been performed on the patient shown in Figure 22. (page 96). The test was carried out one month after the last operation. Symmetry is well-nigh perfect. Sweating is absent on both upper extremities, up to a point on the arms opposite the axillae. A minor difference in the line of demarcation is present. Sweating is present on the face. The band of anhidrosis across the back is seen in Figure 23. (page 97). The close similarity in the shape of the band on both sides is well seen.

Just over three years later, although some sweating is present in the previously anhidrotic area, the line of demarcation is still well-marked and is closely similar to the previous line of demarcation. (Figure 24. - page 97).

Five months later, however, a marked change is present.

/Posteriorly

ii. Raynaud's Phenomena - late results.

Five patients are included in this group. Sympathectomy had been performed two to nine years previously. The type of sympathectomy, however, varied considerably.

Telford's operation had been performed elsewhere on the patient depicted in Figure 14. (page 88) and Figure 15. (page 89) nine years before. Sweating is profuse on both hands and arms, although it appears to be absent on the left thumb. Clinically, too, sweating is not perceptible on this digit. Sweating appears less on both shoulders but is present on both sides of the face. No line of demarcation is present separating any area of anhidrosis anteriorly. Posteriorly, sweating is present on both arms and on the lower part of the shoulders. On the superior aspect of each shoulder, however, sweating is absent. This is more apparent on the left side. A well defined line of demarcation is present, particularly on the left side. This line appears to be slightly lower than the line of demarcation on the right.

Figure 16. (page 90) depicts the sweating test on a patient after bilateral sympathectomy of the upper extremities by cauterisation of the second thoracic ganglia only. Sweating is completely absent on both upper extremities, upper chest and face. The posterior aspect is shown in Figure 17. (page 91). Both anteriorly and posteriorly perfect symmetry appears to be present. The line of demarcation on both aspects is fairly well defined and represents a straight horizontal line. Figure 18. (page 92) shows the posterior aspect three years later. No area of anhidrosis is present. The line of demarcation has disappeared. On the anterior aspect, too, sweating is present on all areas and no distinction can be drawn between sympathectomised and normally innervated skin.

Figure 19. (page 93) represents the sweating pattern on a patient within six months of sympathectomy of the upper

/extremities

FIGURE 14.

Telford's operation nine years previously.

Anterior Aspect.

Note the left Horner's Syndrome.

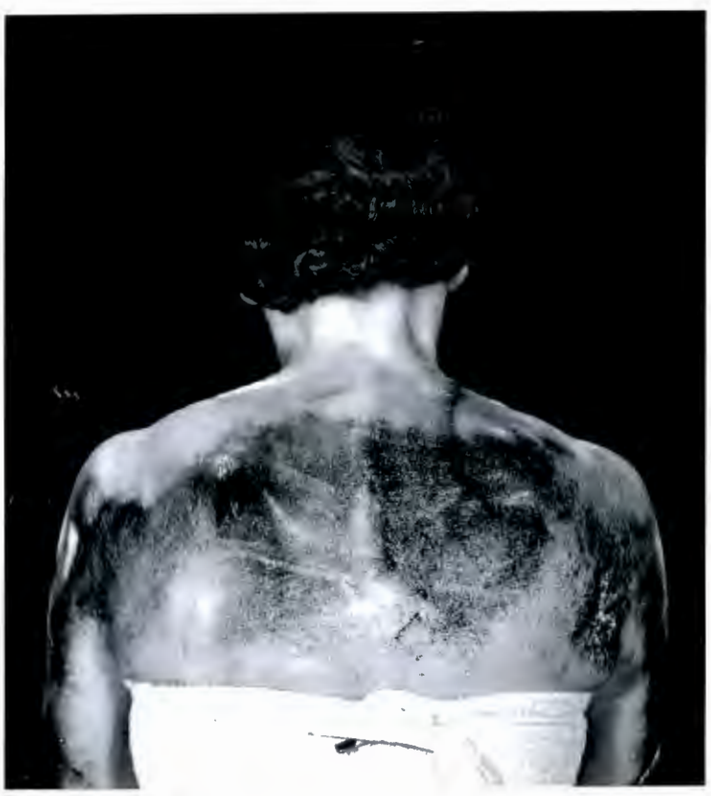


FIGURE 15.

Same case as in Figure 14.

Posterior Aspect.

FIGURE 16.

Four weeks after bilateral cauterisation of Th.2.

Anterior Aspect.

FIGURE 17.

Same case as in Figure 16.

Posterior Aspect.

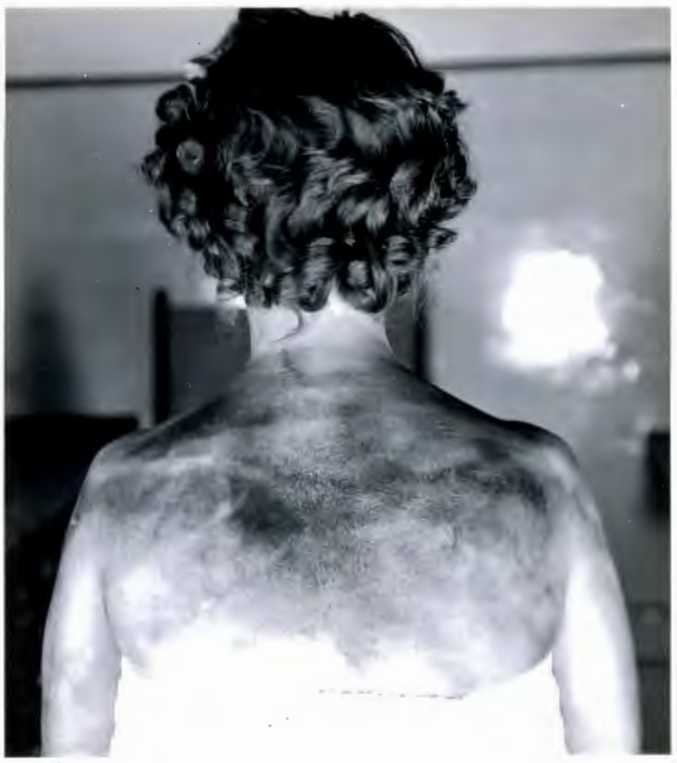


FIGURE 18.

Same case as in Figure 17.

Three years later.

FIGURE 19.

Six months after removal of Left Th.2 and cauterisation of Right Th.2.

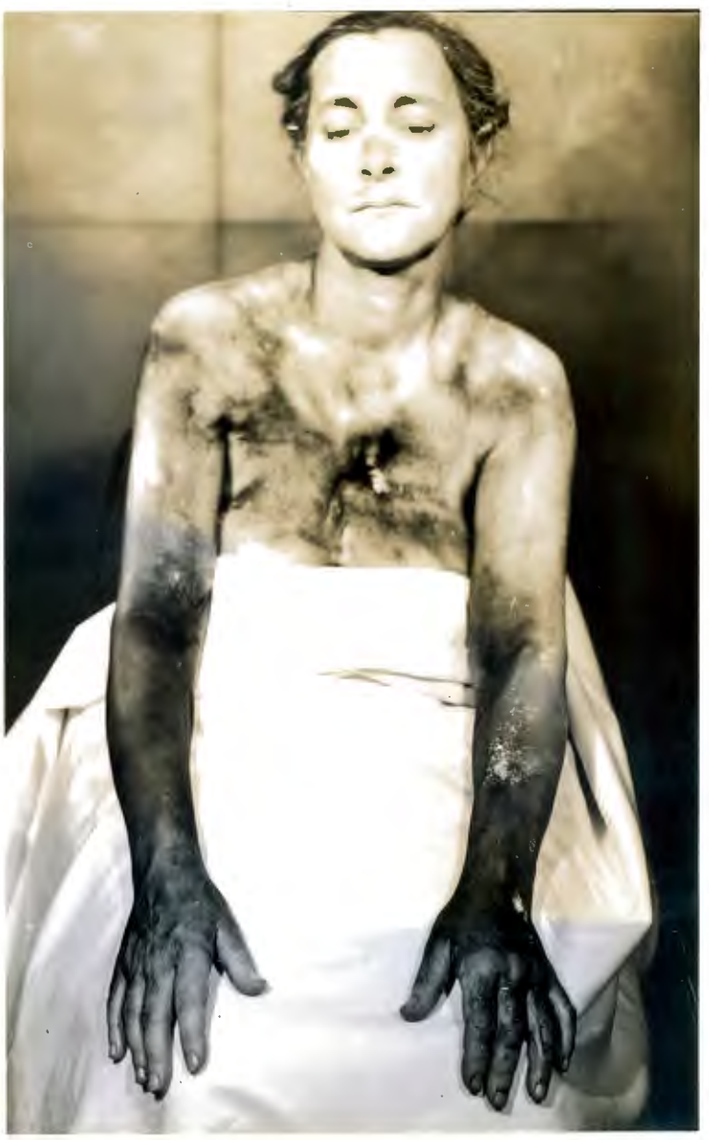


FIGURE 20.

Same case as in Figure 19.

Three years later.

FIGURE 21.

Three years after removal of
Right and Left Th.2.

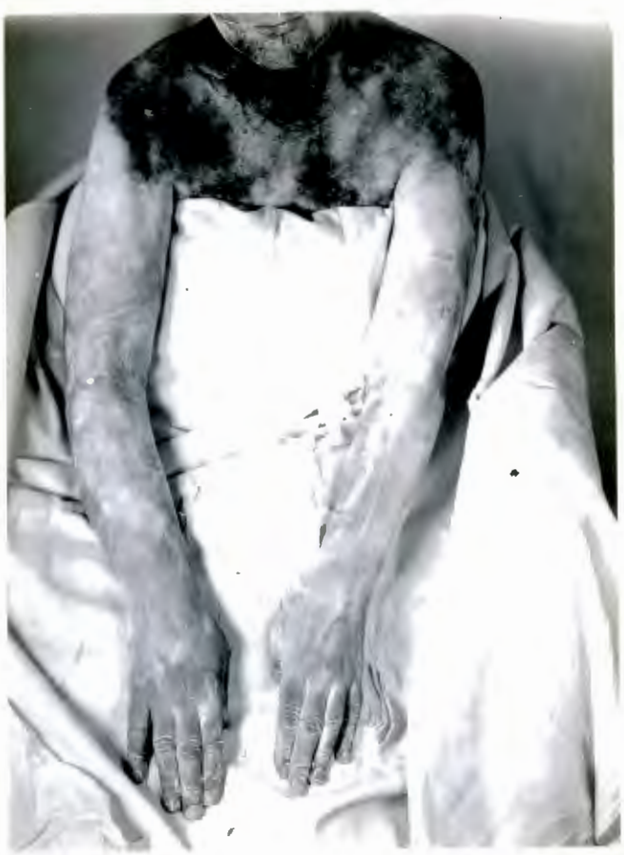


FIGURE 22.

One month after bilateral cauterisation of Th.2.

Anterior Aspect.

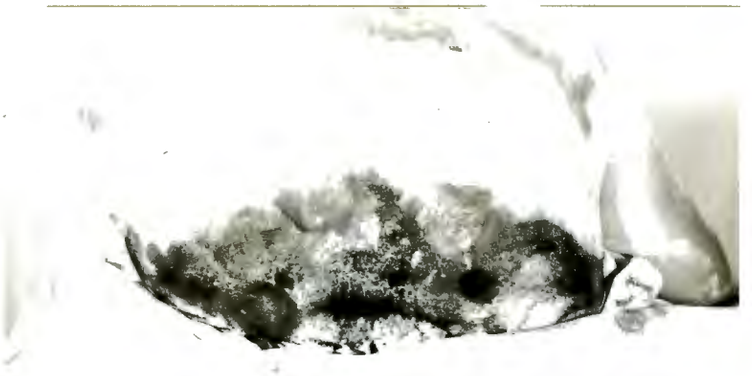


FIGURE 23.

Same case as in Figure 22.

Posterior Aspect.

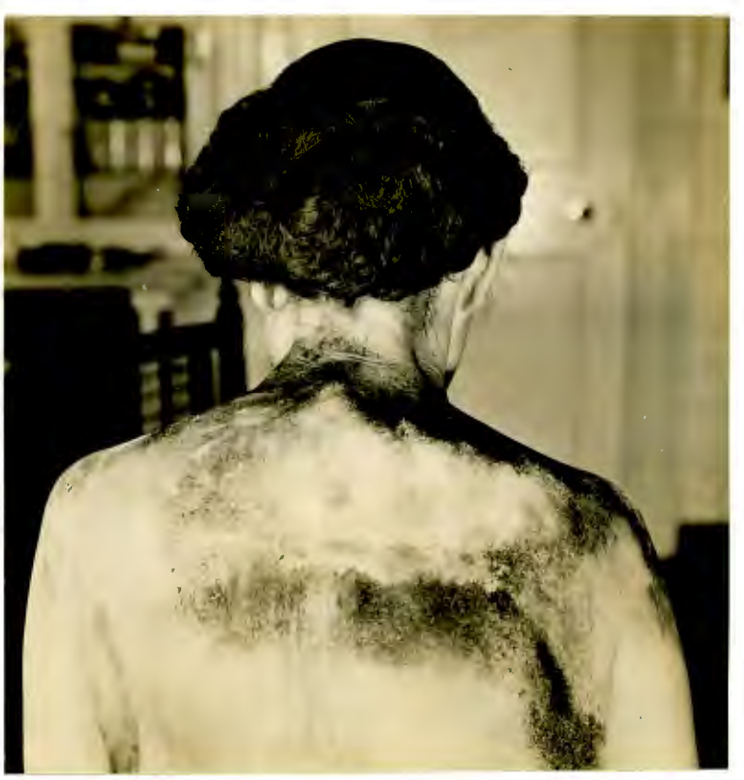


FIGURE 24.

Same case as in Figure 22.

Three years later.

Posterior Aspect.

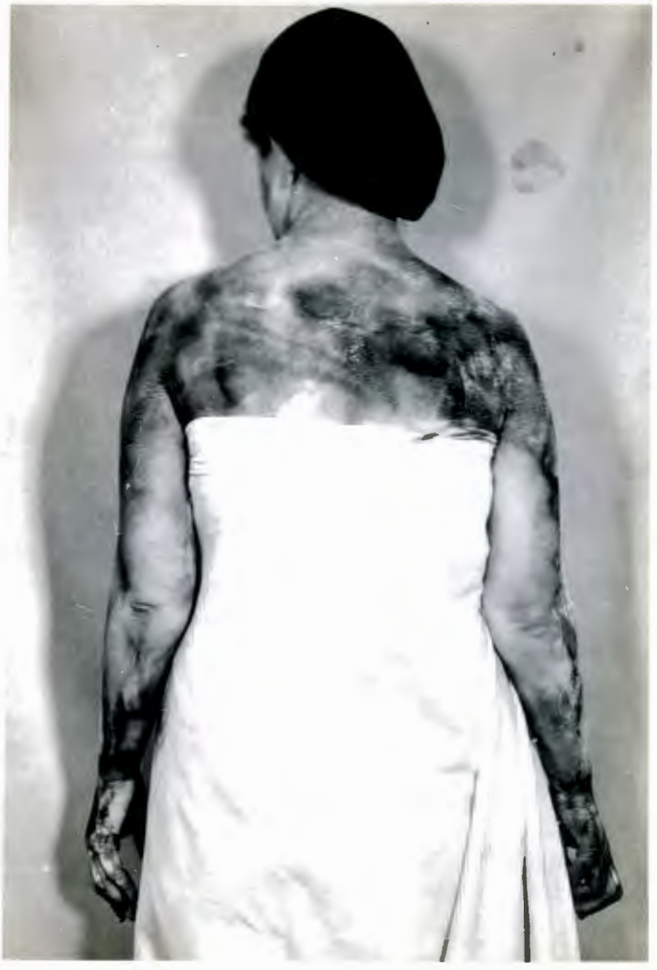


FIGURE 25.

Same case as in Figure 22.

Another five months later.

Posterior Aspect.

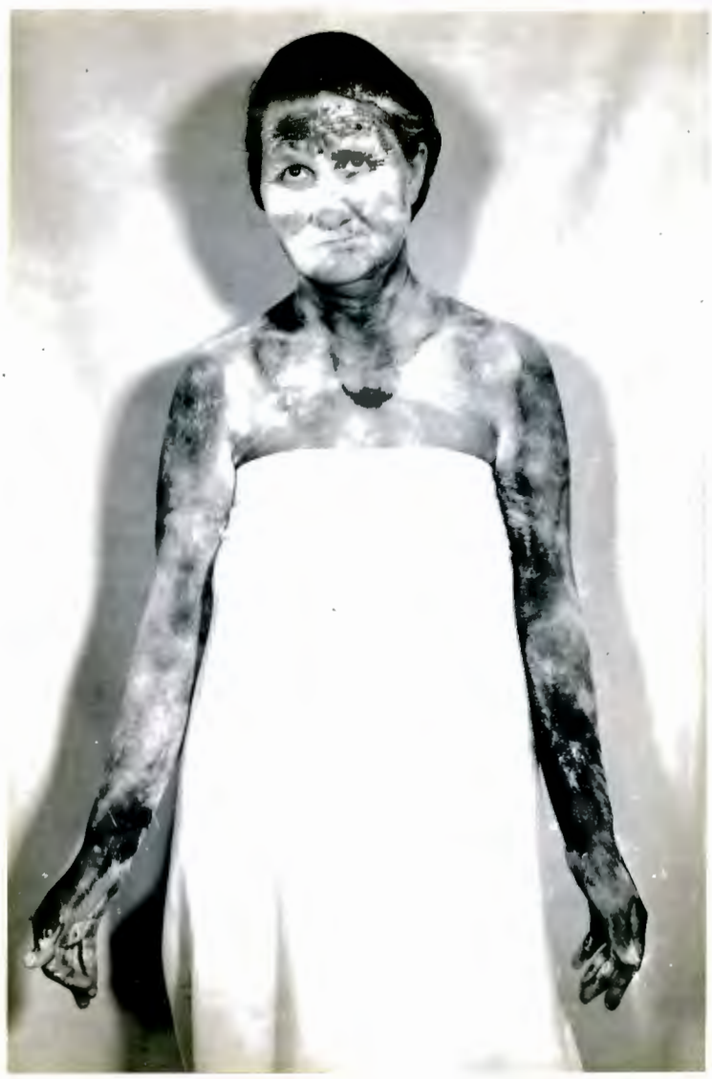


FIGURE 26.

Same case as in Figure 25.

Anterior Aspect.

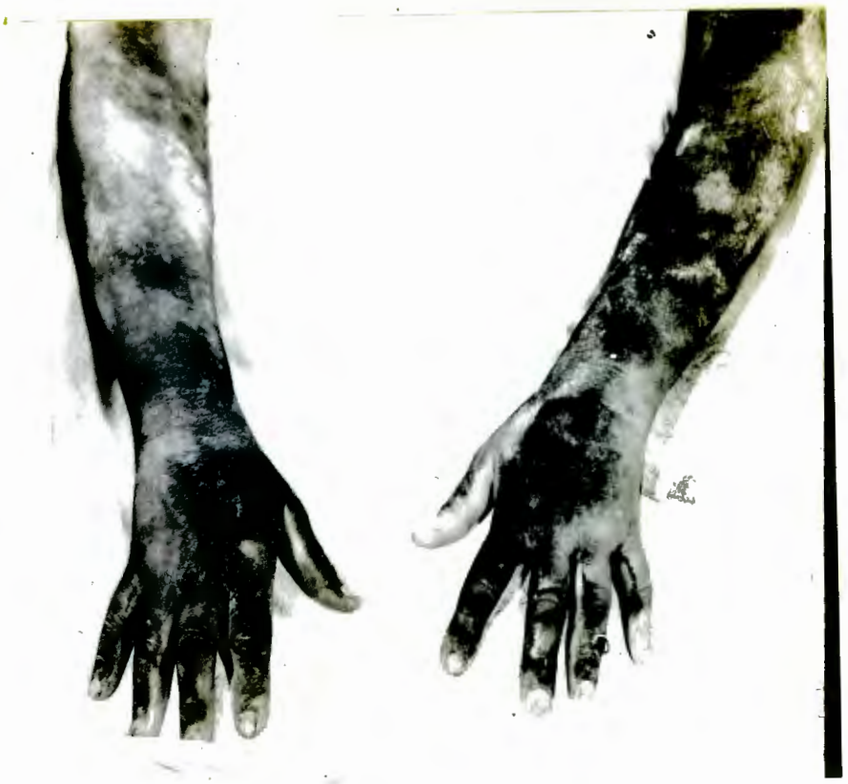


FIGURE 27.

Same case as in Figure 25.

Hands.

iii. One case of Thrombo-angiitis Obliterans had had right stellatectomy performed nine years previously. The sweating pattern after body heating is seen in Figure 28. (page 102). Sweating is present on the normally innervated left side of the face and neck and extends to the midline. The right face and forehead are completely anhidrotic. The line of demarcation extends on to the chest about three inches below the clavicle. However, faint traces of sweating are present on the chest wall. No evidence of sweating is present on the fingers, thumb and dorsum of the hand. The apparently black area on the hand and forearm is due to a tattoo mark.

The remaining subject is the case of causalgia sympathectomised in 1917, by removal of the stellate and second thoracic ganglion on the left side. Figure 29. (page 103) represents the anterior surface of the body after thirty minutes body heating. Sweating is completely absent on the whole of the left upper extremity, shoulder, neck and face. The normally innervated right side shows up strikingly in contrast. The anhidrotic zone extends to the midline only and to a level about two inches above the nipple. Sweating is present in the left axilla and is also present on the adjoining medial surface of the arm. The line of demarcation is strikingly sharp. The posterior aspect also reveals the sharp line of demarcation between the anhidrotic sympathectomised area and the normally innervated sweating area. Starting at the fifth cervical spine, the line extends down to the upper border of the axilla, which here too is also sweating. (Figure 30. - page 104).

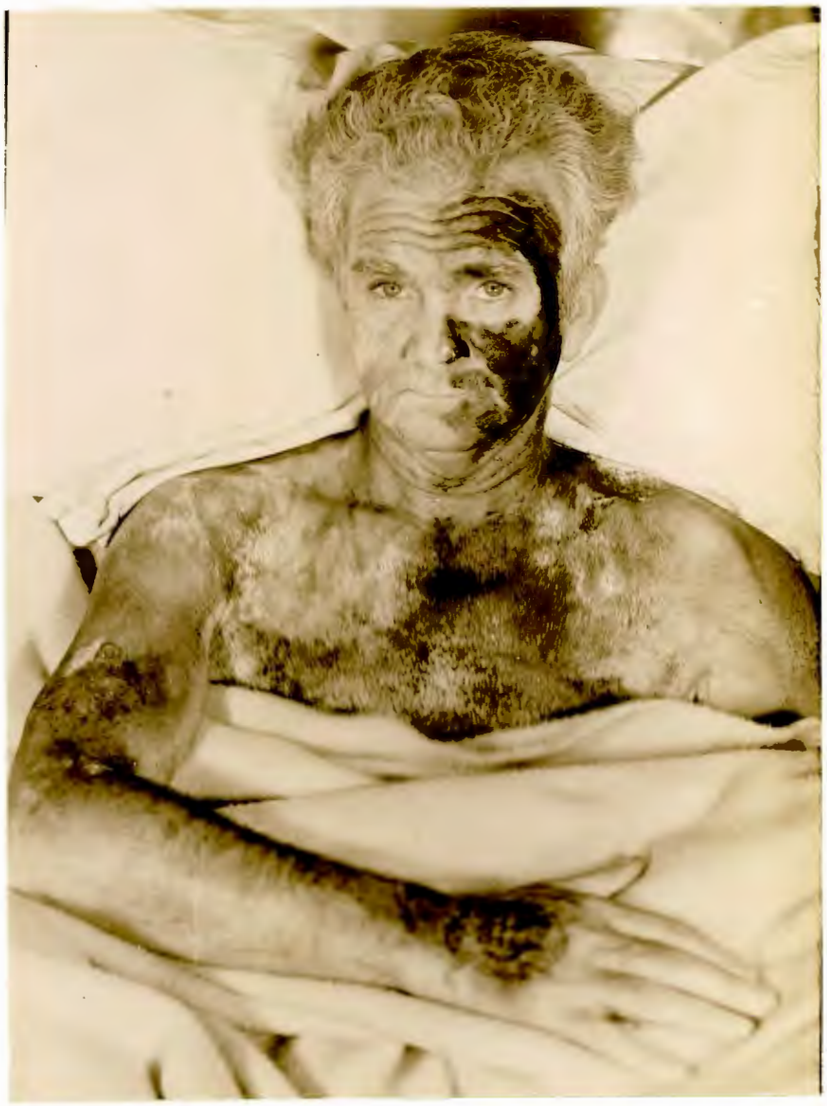


FIGURE 28.

Nine years after removal of
Right Stellate Ganglion.

FIGURE 29.

Thirty years after removal of
Stellate and Th.2 Ganglia

Anterior Aspect.

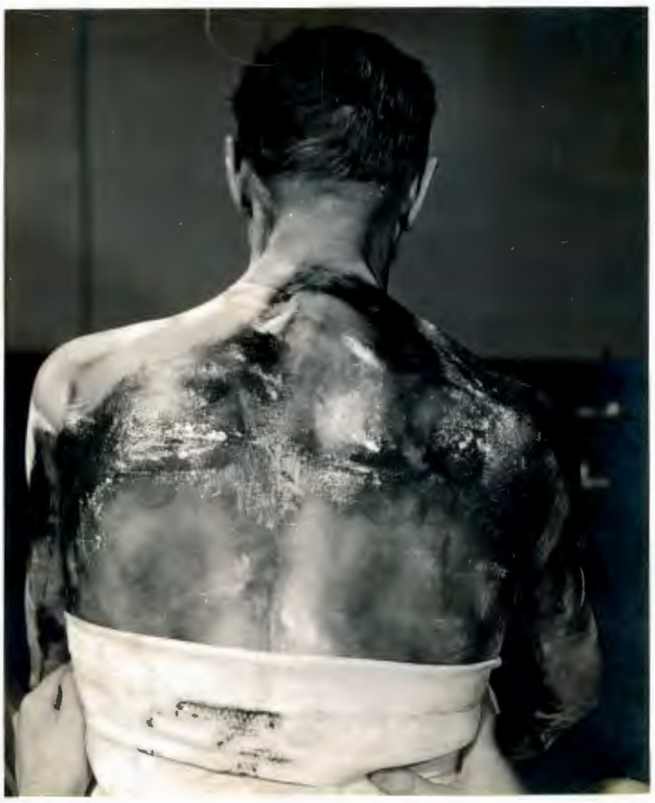


FIGURE 30.

Same case as in Figure 29.

Posterior Aspect.

Summary and Discussion.

All cases of Raynaud's Phenomena observed within six months of sympathectomy show absolute areas of anhidrosis on body heating as demonstrated by the Starch-Iodine Sweating Test.

In those five cases observed three years previously on which sweating tests had been performed, sweating was absent on the extremities in four. One patient showed sweating after sympathectomy had been carried out. In these cases cauterisation had been the method of sympathectomy.

Three years later the pattern shows that sweating now occurs on what was apparently denervated skin. This sweating, however, showed a tendency to be patchy in nature. In one case the arrangement of the sweating pattern seemed to spare the ulnar surface of both extremities. In this case the line of demarcation as shown immediately after operation is still present three years after sympathectomy, although some sweating could be observed in the previously anhidrotic area.

Five months later the line of demarcation had completely disappeared. Sweating was now uniform through "sympathectomised" and normally innervated skin.

In two cases, not included under Raynaud's Phenomena, sweating was absent in the denervated area of skin, even though nine and thirty years had elapsed after stellatectomy.

The extent of sympathectomy seems to play some part in the areas of anhidrosis produced. Four of the five cases included in the "late results" had been sympathectomised by removal of the second thoracic ganglion only. Cauterisation of the second thoracic ganglion resulted in anhidrosis of the arms as far as the axilla in one patient. (Figure 22, page 96). The face and upper chest sweated. Very little

/difference

difference could be seen on either side. In yet another case (Figure 16. - page 90), the same procedure resulted in anhidrosis of the face as well as the upper chest. In one other patient cauterisation of the right second thoracic ganglion did not produce anhidrosis of the hand or forearm. Anhidrosis resulted, however, on the face and neck. (Figure 19. - page 93). When the second thoracic ganglion was removed by open dissection on the left, sweating still occurred on the upper extremity. The area of anhidrosis, however, extended lower than on the right side.

In the remaining patient Telford's operation, i.e. division of the sympathetic trunk below the third thoracic ganglion with ramisection of the second, left an area of anhidrosis on the shoulders only. Both hands sweated. (Figure 14. - page 88).

Thus, although in two cases cauterisation of the second thoracic ganglion resulted in anhidrosis of the upper extremity immediately after operation, the extent of anhidrosis varied in the two cases. Cauterisation of the same ganglion in another patient failed to produce anhidrosis of the upper extremity and when the ganglion was dissected out on the other side, anhidrosis still was not complete.

The late results of these and the other cases where the second thoracic ganglion only was removed, indicated that sweating may re-establish itself shortly after "sympathetic denervation" of the upper extremity by such a procedure.

It has been noted above, that all the patients examined under the "immediate results" had been sympathectomised by removal of the second, third and fourth thoracic ganglia. The areas of anhidrosis produced by this procedure varied not only from patient to patient, but where the operation had been performed bilaterally, differences occurred on

/the two sides

the two sides in the same patient.

Figure 8. (page 79) and Figure 13. (page 84) show the areas of anhidrosis in two patients resulting from bilateral removal of the chain and the above three ganglia. In each case the anhidrotic area extends lower on one side. The shoulder is free of sweating in both cases; both axillae are free in one case, whereas one axilla sweats in the other. Similarly, whereas the right side of the face does not sweat in the patient shown in Figure 8. (page 79), the left side sweats (Figure 9. - page 80).

In one patient the posterior aspect showed a fairly close similarity in the two sides (Figure 6. - page 77) but, anteriorly, a slight difference is present on the upper chest. (Figure 5. - page 76). On this aspect, too, the left side of the face sweats whereas the right does not.

A close similarity exists in the areas of anhidrosis resulting in the two patients shown in Figure 4. - (page 75) and Figure 31. (page 109) yet the axilla sweats in the one but not in the other. In these two patients sweating does not occur in the face.

In those patients suffering from Raynaud's Phenomena, the immediate results of removal of the second thoracic ganglion only or the second to the fourth thoracic ganglia inclusive, show that out of nine such patients anhidrosis of the upper extremity occurred in eight. In the remaining patient the hands still sweated. In this patient, however, some doubt was present, at the time of operation, as to whether the second ganglion had been removed.

In the patient sympathectomised for causalgia by removal of the stellate and second thoracic ganglia, sweating occurred in the axilla but not on the rest of the arm except for an area on the medial aspect.

/A fairly close

A fairly close similarity exists in the pattern of anhidrosis resulting from removal of the stellate ganglion with or without the second thoracic ganglion. (Figure 29. - page 103, Figure 28. - page 102, Figure 32. - page 110). Similarly, on the posterior aspect the lines of demarcation are very much alike in all three. (Figure 15. - page 89, Figure 30. - page 104, Figure 33. - page 111). The patient in Figure 15. (page 89) is included in the Raynaud's group. A left Horner's Syndrome has persisted after Telford's operation.

FIGURE 31

After removal of Left Th.2, Th.3 and Th.4 in a case of Raynaud's Phenomena secondary to Rheumatoid Arthritis.

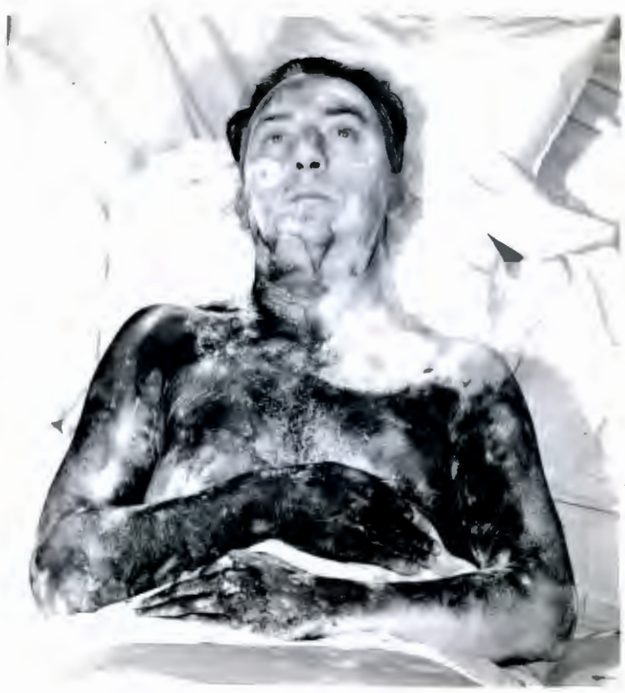


FIGURE 32.

A case of "traumatic" stellatectomy
following numerous operations
on a compound fracture
of the left clavicle.

Anterior Aspect.

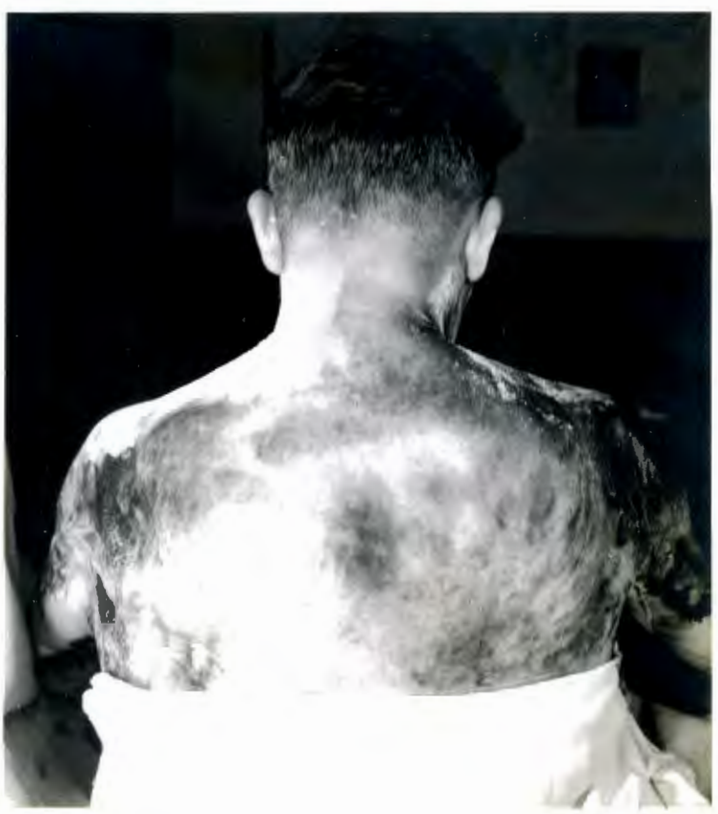


FIGURE 33.

Same case as in Figure 32.

Posterior Aspect.

Conclusions.

Immediate results of sympathetic denervation of the upper extremity in cases of Raynaud's Phenomena show anhidrosis of the extremity with the Starch-Iodine Sweating Test.

Late results show the presence of sweating on the extremities in all these cases.

A case of Causalgia still has anhidrosis of the upper extremity thirty years after removal of the stellate and second thoracic ganglia. A case of Buerger's Disease has anhidrosis of the upper extremity nine years after removal of the stellate ganglion.

The upper level of the preganglionic sweat fibres to the hand appears to be the second thoracic ganglion in all cases examined. Removal of the second thoracic ganglion, however, does not result in a permanent anhidrosis.

It is apparent that removal of the stellate ganglion plus the second thoracic ganglion would result in a permanent denervation of the upper extremity. Should the axilla have to be included in the anhidrotic area, the third and fourth ganglia also should be removed.

2. Skin Resistance.

The resistance offered by the skin to the passage of a minute imperceptible current through the body is localised almost entirely in the skin. It has been shown that a puncture made through the skin with a hypodermic needle reduces the resistance from any level to practically zero. (Richter - 1924).

This skin resistance is controlled largely through the nervous system. Section of a peripheral nerve produces a great increase in the resistance of the skin supplied by that nerve. (Richter - 1929, Richter and Katz - 1943, Richter - 1946). Stimulation or irritation of the nerve has the opposite

/effect producing

effect, producing a decrease in the skin resistance.

That the skin resistance depends on the sympathetic component of the peripheral nerves has been shown by Richter and Tower (1931, 1932). Sympathectomy, by sectioning the preganglionic rami of the stellate ganglion in the cat, produces as great an increase in skin resistance as does section of the entire nerve trunk. Richter (1929) showed that factors stimulating the sympathetic nervous system, such as muscular effort, emotional excitement or mental tension, tend to decrease skin resistance. Factors decreasing sympathetic activity, such as rest, sleep and relaxation, tend to increase skin resistance.

Skin resistance varies directly with sweat gland activity, becoming low when the sweat glands are active and high when they are inactive. (Richter - 1924, Richter and Whelan - 1943). However, these changes do not depend on the presence of moisture on the skin, but on actual changes occurring in the sweat glands themselves. (Richter - 1946).

Normally innervated skin shows, under ordinary conditions, distinct regions where the resistance is high and others where it is low. (Richter, Woodruff and Eaton - 1943). Thus low readings are obtained for areas with a rich sweat gland supply, e.g. palms of the hands, face, axillae, cubital fossae. These areas change in shape with the various physiological changes which effect the entire body. On exposure to heat the areas enlarge and merge finally into one area of low resistance which includes the entire surface of the body. On exposure to cold the reverse obtains and only high resistance remains.

By means of the skin resistance, it is possible to define on any part of the body areas of skin affected by

/sympathectomy

sympathectomy - thoracic, lumbar or thoraco-lumbar. Such areas have an abnormally high resistance. By sympathectomy the sweat glands are denervated and it is through this that the skin resistance is so high. Carmichael et al (1941), however, claim that not only is the skin resistance dependent upon sweating but it is also dependent upon the synchronous development of vasoconstriction. The response occurs when either of these components is present but is abolished when both are absent.

The method, as a test of sympathetic activity, has been greatly developed recently, especially by Richter and his co-workers. According to Richter and Woodruff (1942, 1945), the denervated areas, as demonstrated by the resistance method, correspond closely to areas which do not sweat as shown by the Minor Starch-Iodine sweating test.

Actually, compared to the Minor Starch-Iodine sweating test, the determination of the skin resistance is simple and involves less time and discomfort for the patient; it can be used on coloured as well as on white patients and on individuals who do not sweat sufficiently to colour the starch paste.

Method.

The technique adopted in this series differs very little from that used by Richter and his colleagues. (1943, 1946). The apparatus used (Figure 34. - page 116) consisted of:

i. 4½ volt battery.
ii. Mirror galvanometer.
iii. Two electrodes.
iv. A slit lamp.
v. Resistances of various strengths.

The one electrode has the shape of a clip. By means

/of a specially

of a specially devised clasp it can be firmly fastened to the lobe of the ear in such a way that the disc of the electrode rests directly over the front surface of the ear lobe. This electrode remains fixed throughout the examination.

The other electrode consists of a zinc disc which is built into the end of an insulated handle. This electrode is used by the examiner to bring the flat, smooth surface in contact with the skin on any part of the body.

All these parts are connected in series and the deflections of the galvanometer are projected on to a scale. It was possible to graduate the resistance of any part by means of a standard resistance box. Resistances of 500,000 Ohms and more were considered to be significant of sympathectomised skin and the instrument was standardised accordingly.

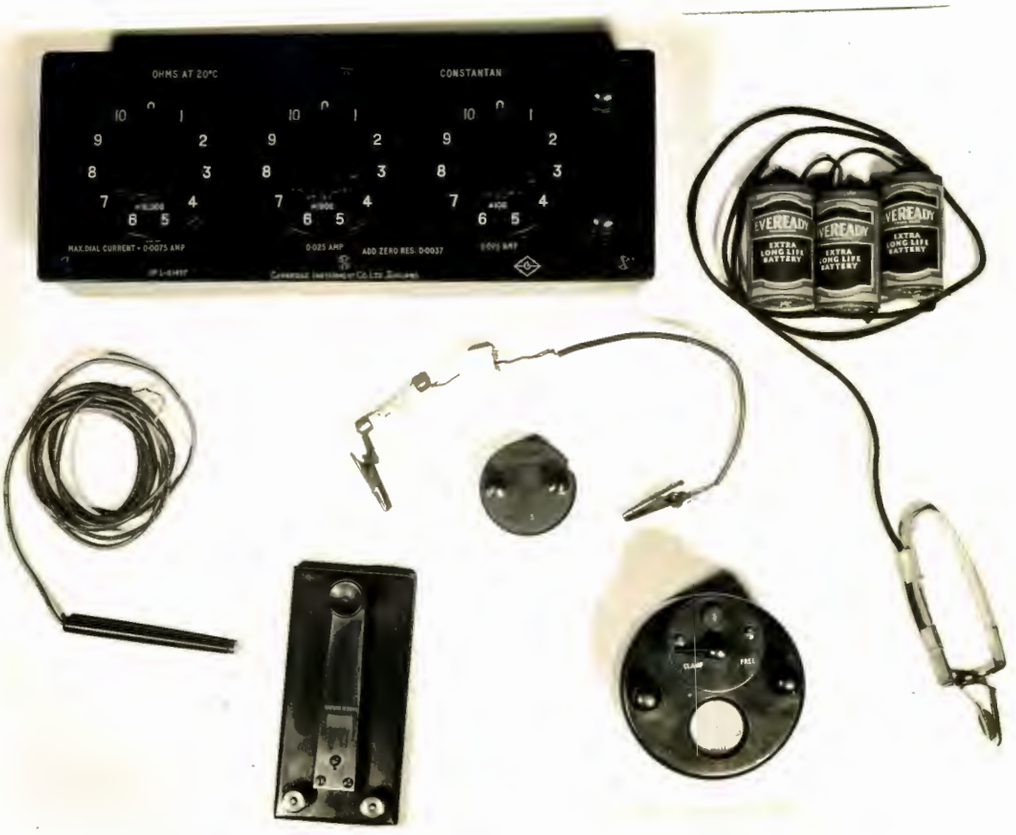

OHMS AT 20°C
CONSTANTAN
MAX.DIAL CURRENT = 0·0075 AMP
0·025 AMP
ADD ZERO RES. 0·0037
EVEREADY
EXTRA LONG LIFE BATTERY

FIGURE 34.

Technique.

The patient was heated for a few minutes by immersing both feet in water at 43°C. The patient was completely covered with one or two woollen blankets. This method of heating is adopted to make the resistance of the contiguous normally innervated areas as low as possible. The heat has little or no effect on the resistance of the denervated areas of skin. Systemic measures such as aspirin or hot tea may be used either separately or in combination with heating. (Richter - 1946).

Injection of pilocarpine can be used as a means of lowering normal skin resistance but Richter (1946) found that pilocarpine does not give constant outlines of areas denervated by sympathectomy.

The ear electrode is placed in position after the skin of the ear has been punctured by a fine needle. This puncture eliminates the resistance of the skin under the electrode. Before applying the electrode a paste, such as that used under the electrodes of electrocardiographs, was applied to the skin of the ear lobe. As a result of the elimination of the resistance under the ear lobe by the skin puncture, all of the remaining resistance offered by the body is localised in the skin under the movable electrode held by the examiner.

With one electrode attached to the ear lobe and the other in contact with the skin, the amount of current from the battery that flows through the circuit is indicated by the excursion of the galvanometer. The extent of the excursion varies directly with the resistance offered by the skin under the movable electrode. When this resistance is

/high the mirror

high the mirror will not deflect, indicating that no current is flowing. When the resistance is low the mirror moves quickly across the scale indicating that a large amount of current is flowing.

The full current from the battery is turned on by means of the switch. The flat surface of the movable electrode is held against any normally innervated area of skin, e.g. the chest and abdominal wall. If the deflection of the galvanometer is across the scale and is rapid, the patient has been heated sufficiently for the test. Should this not occur and the response be small, the patient is heated for a longer period.

As soon as a place is found where no deflection results, it is known that a denervated area is located.

The electrode is then allowed to slide along the skin surface, taking care to keep all the flat surface in contact with the skin. The electrode must be used with extreme gentleness. Any undue pressure on the skin under the electrode lowers the resistance of that particular part. The point where there is a sudden rise from a high resistance to an area of low resistance is marked on the skin and by tracing out the pattern so drawn the denervated areas can be mapped out quite easily. The line of demarcation is usually fairly sharp.

In several patients it was noted that areas in the face consistently gave readings of low resistance, in spite of being denervated. It was particularly so on the forehead and cheek. Whilst there was certainly no evidence of active sweating, it is possible sweating actually was present in those "denervated" areas.

In some cases the resistance drops to a lower level than in the main sympathectomised areas but not down to the level of the resistance of the rest of the body. Such areas

/of partial

of partial decrease in skin resistance must indicate, according to Richter and Woodruff, that some sympathetic innervation still remains. They termed such areas "zone" areas and attribute them to overlapping of the distribution of the adjacent dermatomes.

In this series, only the upper extremities were tested. This includes the head, neck, arms and hands. The lowest reading taken was just below the nipple in all cases.

The current is below the range in which it could be felt by the patient. However, the sudden fall in resistance from over 500,000 Ohms to a few thousand Ohms made it difficult always to make certain that the current remained imperceptible. The first tingling sensation reported by the patient usually came simultaneously with the drop in resistance. This sensation may actually be painful and was not infrequently felt about the face.

Results.

The skin resistance test was performed on twelve patients in this series. Ten patients had been sympathectomised for Raynaud's Phenomena, one for Thrombo-angiitis Obliterans and one for Causalgia.

Of those patients with Raynaud's Phenomena, five were tested shortly after sympathectomy, i.e. within the first six months, and five were tested at various intervals, but not earlier than one year after operation.

A uniform pattern was adopted to depict the areas of high resistance, i.e. sympathectomised areas, in the whole group. (Figure 35. - page 128). It was felt that if the resistance was 500,000 Ohms or more, the skin area was denervated, i.e. not under sympathetic control. These areas of high resistance are shown as black in the figures. Anything

/that is not so,

that is not so, and is represented by the various crossed, oblique, vertical and horizontal lines, is not considered sympathectomised.

The cases suffering from Raynaud's Phenomena were once more classified in two groups:-

1. Immediate - within six months of sympathectomy.

In all these cases sympathectomy was standard in that the second, third and fourth thoracic ganglia had been removed or cauterised.

Figure 36. (page 129) represents the pattern traced fourteen days after right sympathectomy. The whole of the right upper extremity appears sympathectomised. The area of high resistance starts at the midline. The lower part of the face and upper part of the neck show an area of low resistance like that of normally innervated skin. Sweating was not clinically perceptible at this point. The non-sympathectomised left upper extremity shows two large areas of high resistance. Sweating was present in these parts at the time of testing. Six weeks later, i.e. after sympathectomy of the opposite extremity, the pattern had changed. (Figure 37. - page 130). Both forearms and hands showed high resistance areas only. About both cubital fossae the resistance was low. The line of demarcation previously present has completely disappeared. Areas of low resistance now appear on the right chest and shoulder. There is no evidence of areas of high resistance in the face and forehead on either side. In spite of the areas of low skin resistance about both cubital fossae and the axillae, both extremities are still sympathectomised six weeks after sympathectomy.

The result of sympathectomy eleven days after operation is shown in Figure 38. (page 131). The whole of the left upper extremity has a high resistance. This area of high resistance extends to the midline. The line of demarcation

/is sharp

is sharp. The lower level is below the nipple. The face, however, has a low resistance, only the left side of the forehead appears sympathectomised as judged by this test, but even on the forehead the line of demarcation is sharp and well defined. On the posterior aspect the appearance is the same. The whole upper extremity from just below the hairline in the neck to below the scapula has a high resistance. The sharpness of the line of demarcation in the midline indicates the extent of the sympathectomised areas. (Figure 39. - page 132).

The areas of skin sympathectomised, as judged by the skin resistance, coincide remarkably with that shown by the Starch-Iodine test. The area of anhidrosis, as judged by the latter test, is shown in Figure 3. (page 74) and Figure 4. (page 75). The only difference is the lower level of high resistance on the posterior aspect of the patient. Sympathectomised skin appears to be just below the inferior angle of the scapula, whereas in the sweating test the line of demarcation passes through the body of the scapula.

The pattern produced by mapping out the areas of skin resistance on the third patient one month after sympathectomy of the left upper extremity by removal of the second, third and fourth thoracic ganglia, is shown in Figure 40. (page 133). The right upper extremity had been sympathectomised in the same way two months previously. The posterior aspect only is shown. The resistance is high on the right side, but on the left side this is not so. The line of demarcation in the midline is sharp, and distinct. The resistance of the left upper extremity lay between 100,000 and 500,000 Ohms, but whilst this is higher than other normally innervated skin areas, the difference between the two sides is convincing. The test was repeated four

/months later

months later. On this occasion both upper extremities appear sympathectomised after body heating had been performed. The whole of both limbs are included in the area of high resistance. No difference is seen on the two sides, except for an area of low resistance on the forehead and upper face. In these sites a sharp line of demarcation is present in the midline. (Figure 41. - page 134). The evidence of whether the left side is sympathectomised or not is conflicting, for the right side consistently shows a high resistance. Starch-Iodine sweating tests show that sweating is present on the left side of the forehead and face. But sweating is also present on the left neck and shoulder which show high resistance. (Figure 9. - page 80).

The remaining patient in this group had been sympathectomised five days before examination. The sympathetic supply to the left upper extremity had been interrupted by removal of the second, third and fourth thoracic ganglia. Pilocarpine gr.1/6 was administered intramuscularly and shortly after the secretory effects became manifest, the resistance was estimated. Areas of low resistance were found to be present over the whole forehead and face. As far as the angle of the jaw resistance was low. The neck and both shoulders showed high resistance to the current. The right upper limb revealed a high resistance to just above the elbow. Below this point the resistance was lower. The resistance of the left upper limb was high apart from a small area on the antero-lateral aspect of the forearm. No line of demarcation was present between the two sides on the chest anteriorly. The area of high resistance extended well down on both sides to just above the umbilicus. No distinction could really be drawn between the sympathectomised and normally innervated extremities in this patient after the administration

/of pilocarpine.

of pilocarpine.

In the remaining subject of this group sympathectomy of both upper extremities had been performed six months previously. Figure 42. (page 135) depicts the pattern of skin resistance after body heating. Both upper extremities have a high resistance. These areas of high resistance are uniform and extend on both sides to the neck. The high resistance pattern extends slightly higher on the left side than on the right. The face and neck have a low resistance on both sides. In this patient Th.2, Th.3 and Th.4 were removed on the left side and on the right side Th.2 only. As judged by skin resistance methods both upper extremities appear to be sympathectomised six months after operation.

ii. Late - includes all sympathectomies performed one year or more prior to examination.

The nature of sympathectomy was the same in four of the patients in this group, i.e. the second thoracic ganglion only was either removed or cauterised; in the fifth patient Telford's operation had been performed nine years previously.

Figure 43. (page 136) depicts the pattern of skin resistance on both upper extremities fourteen months after cauterisation of the left second thoracic ganglion. The area of high resistance extends over the whole of the left upper limb, shoulder and left side of the chest. At the midline a well marked line of demarcation exists where the resistance is lower. The area of high resistance extends on to the face but the forehead has a low resistance. Here, too, the demarcation is sharp in the midline. On the right side, i.e. the normally innervated extremity, the resistance is lower than the sympathectomised left side.

/however, several

However, several patches of high resistance are present, viz. on the right shoulder and the right thumb. The sharp distinction between the two sides indicates that sympathectomy of the left upper limb, as judged by skin resistance, is still complete fourteen months after operation.

Bilateral cauterisation of the second thoracic ganglion had been performed three years previously on the patient depicted in Figure 44. (page 137) and Figure 45. - (page 138). The skin resistance patterns show that the resistance is uniformly low on both upper extremities. The neck and face show a still lower resistance both on the anterior and posterior aspects. Although the resistance is comparatively higher on the limbs than on the face and neck, comparison with the results shown above indicates that sympathectomy of the two upper extremities, in this patient, is no longer complete. That this is so is confirmed by the Minor Starch-Iodine sweating test. Sweating is present over the whole of the back and shoulders. (Figure 18. - page 92). Three years after sympathectomy of the upper extremities in this patient, skin resistance patterns fail to reveal any denervated areas of skin.

About the same time as the above patient was sympathectomised another patient also had the same type of operation for Raynaud's Phenomena of the hands. The skin resistance pattern of this patient three years after operation is depicted in Figure 46. - (page 139) and Figure 47. (page 140).. On the anterior aspect the only patches of high resistance are on the medial aspect of the right limb, viz. on the elbow and the hypothenar eminence. The resistance of the remainder of both limbs is relatively higher than on the neck and face, but the only areas that can be considered to be denervated are the patches on the medial aspect on the right upper limb. That

/the height

the height of the skin resistance is not due to a technical fault was confirmed by the Starch-Iodine sweating test. Sweating was present on both upper extremities and on the face after thirty minutes body heating. (Figure 25. - page 98, Figure 26. - page 99). In certain areas the degree of sweating is less, viz. the right arm and upper forearm. In this patient, too, skin resistance patterns reveal little, if any, sympathectomised areas to be present three years after operation.

Figure 48. (page 141) and Figure 49. (page 142) depict the patterns of skin resistance in a patient who had had bilateral sympathectomy four years previously. Removal and cauterisation of the second thoracic ganglion was the method adopted on the right and left sides respectively. Anteriorly, areas of high resistance are seen on the lateral aspect of the left arm, the whole palmar surface of the left hand and on the right shoulder. The resistance of the rest of the extremities is relatively lower, whilst on the face and neck it is very low. On the posterior surface the whole dorsum of the left hand has a high resistance. A strip of high resistance is present on the right shoulder which extends across the midline and enlarges to embrace the whole of the left shoulder, extending down the lateral surface of the arm. These areas of high resistance, therefore, are those remaining from the sympathetic denervation four years previously. Comparison with the Starch-Iodine sweating test (Figure 21. - page 95), shows a close similarity. Sweating is absent on the left hand, lateral aspect left arm and on the right shoulder.

The remaining case of Raynaud's Phenomena had had Telford's operation performed bilaterally nine years previously. Skin resistance patterns on the anterior aspect show a small area of high resistance on the right side of the face and forehead. This area extends to the midline. The rest of the

/face,

face, neck and the whole of the upper extremities and upper chest have a low resistance. (Figure 50. -page 143). On the posterior surface an area of high resistance extends across the neck slightly on to the right shoulder, but extends further down on the left side. The remaining areas all have a low resistance. (Figure 51. - page 144). Starch-Iodine sweating tests reveal sweating to be present on all areas of the limbs and face. Sweating was particularly profuse on the limbs. Posteriorly, sweating is absent on the neck and left shoulder. Apart from the right face, a close similarity exists between the skin resistance and Starch-Iodine sweating pattern. (Figure 14. - page 88, Figure 15. - page 89).

iii. Sympathectomy of the right upper extremity by stellatectomy had been performed nine years previously on a patient with Thrombo-angiitis Obliterans. Skin resistance patterns are shown in Figure 52. (page 145). On the anterior aspect the whole of the right hand and forearm below the elbow have a high resistance. The lateral aspect of the right arm and shoulder similarly appear denervated. The remaining areas show low resistance only. The resistance on the posterior aspect is high on the right forearm and hand, with a narrow band of high resistance on the lateral side of the arm and shoulder.

Causalgia was the reason for sympathectomy of the left upper extremity in the remaining patient. The stellate and second thoracic ganglia were removed thirty years previously. The skin resistance pattern is shown in Figure 53. (page 146). The whole of the left upper extremity is covered by an area of high resistance. This area stops short at the midline and extends to just below the nipple. Superiorly, it extends to just above the clavicle. High resistance areas cover the right side of the forehead and upper face. Again, the extension is just to the midline. The left side of the neck and lower face has an area of low resistance intervening.

/between the

between the two areas of high resistance. The difference in the two sides and the extension just to the midline indicates that sympathetic innervation is still absent on the left side of the body. A very close similarity to the skin resistance pattern is revealed by the Starch-Iodine sweating test. (Figure 29. - page 103). Sweating is absent over the whole of the left upper limb, upper chest above the nipple and left side of the neck and face. The only disparity between the tests is the area of low resistance encountered in the neck and face and the fact that the resistance is high to below the nipple whereas anhidrosis extends above the nipple. However, the close similarity between the two tests, in spite of the minor differences, indicates sympathectomy to be still complete, thirty years after operation.

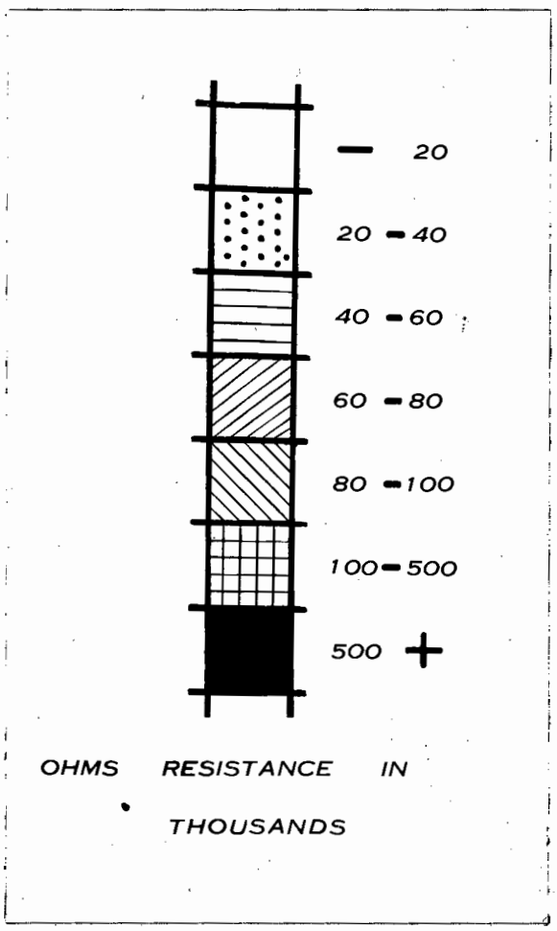

— 20
20 — 40
40 — 60
60 — 80
80 — 100
100 — 500
500 +
OHMS RESISTANCE IN
THOUSANDS

FIGURE 35.

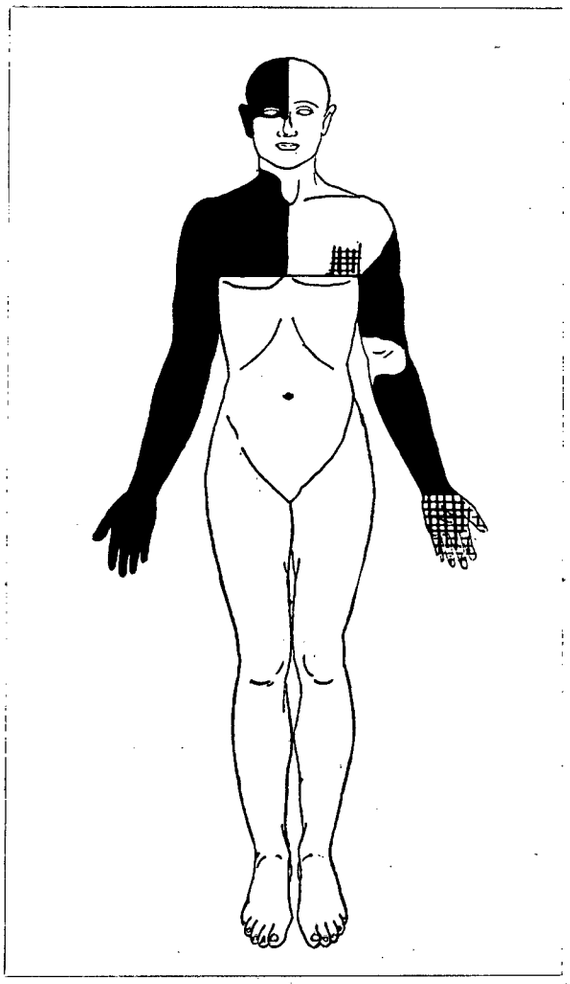


FIGURE 36.

Fourteen days after removal of
Right Th.2, Th.3 and Th.4.

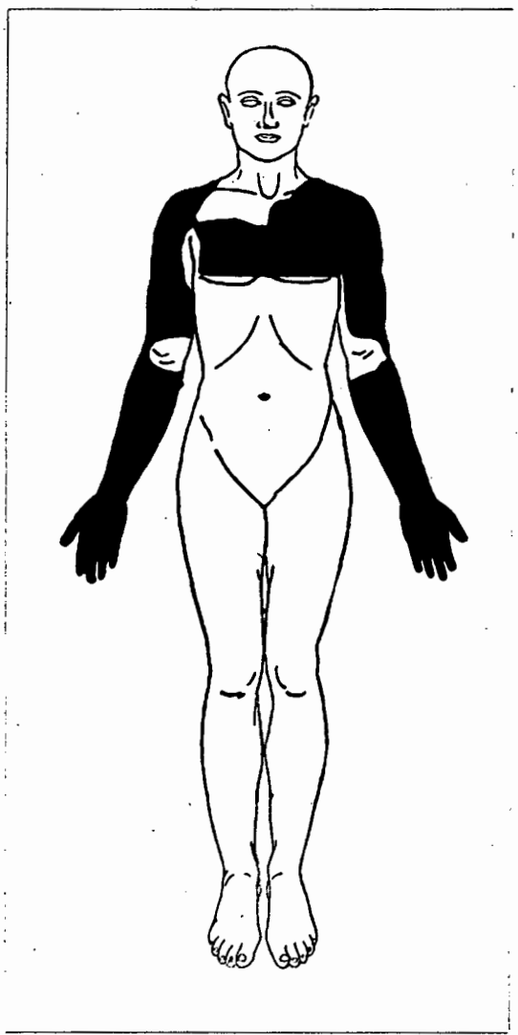


FIGURE 37.

Same case as in Figure 36.

Six weeks later
i.e. eleven days after removal of
Left Th.2, Th.3 and Th.4.

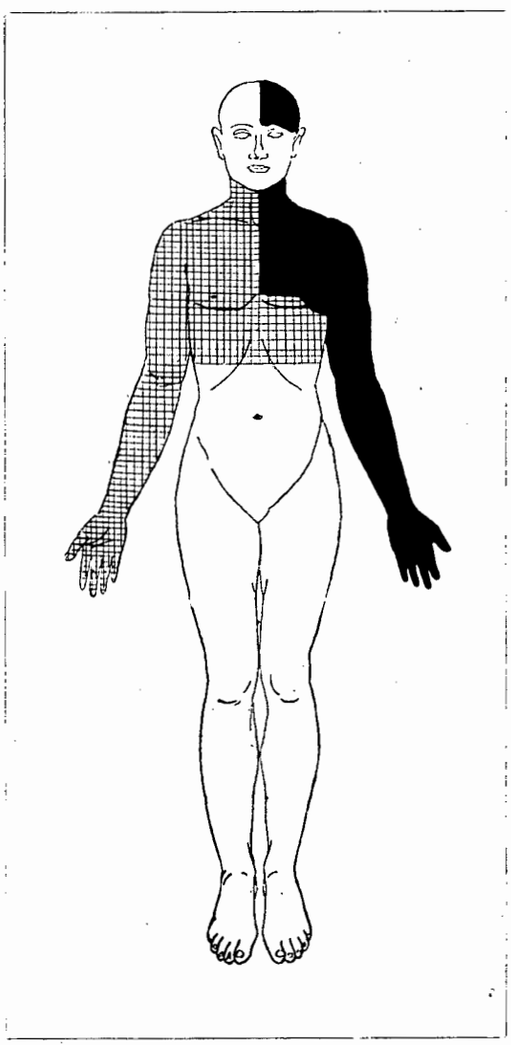


FIGURE 38.

Eleven days after removal of
Left Th.2, Th.3 and Th.4.

Anterior Aspect.

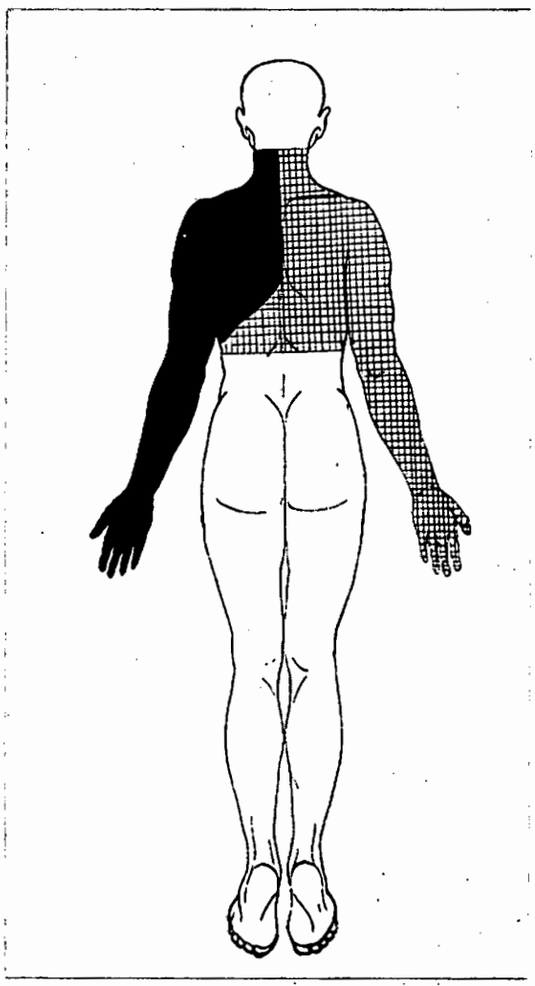


FIGURE 39.

Same case as in Figure 38.

Posterior Aspect.

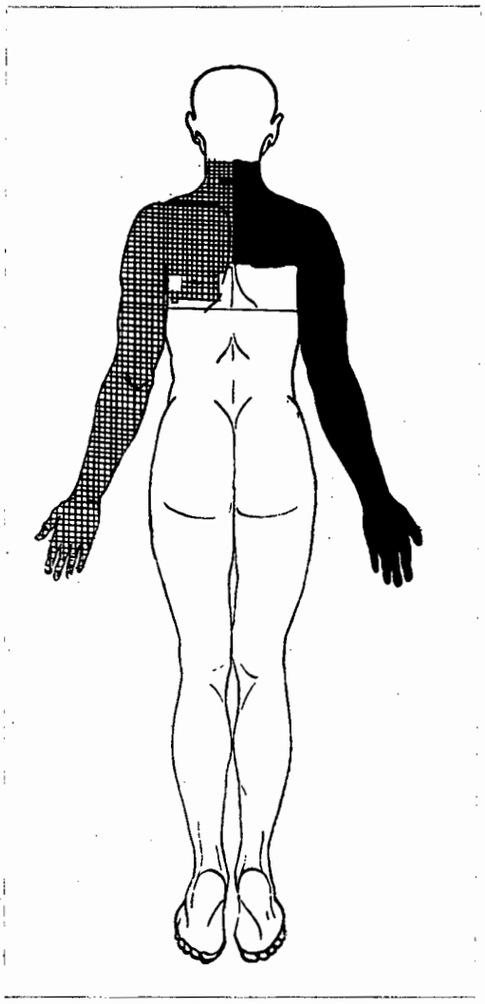


FIGURE 40.

One month after removal of
Left Th.2, Th.3 and Th.4
and
Three months after removal of
Right Th.2, Th.3 and Th.4.

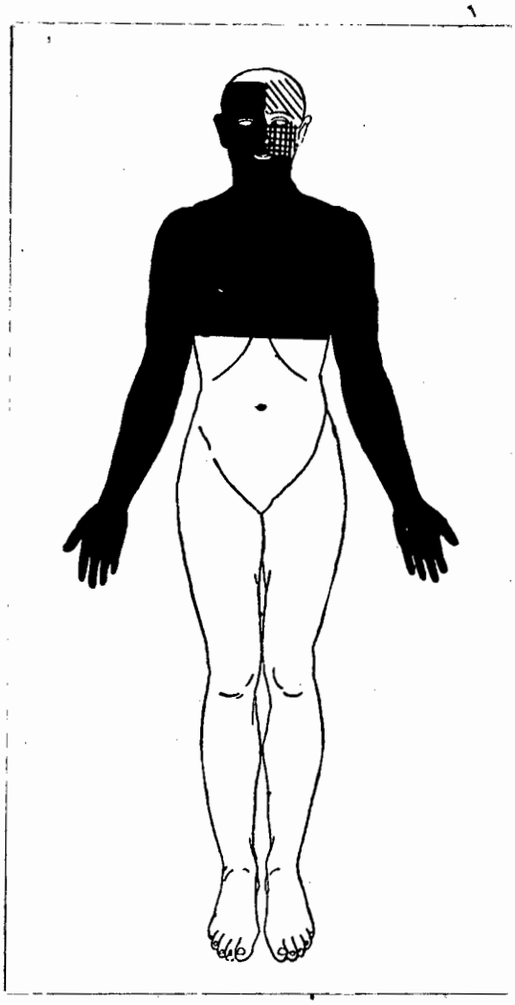


FIGURE 41.

Same case as in Figure 40.

Four months later.

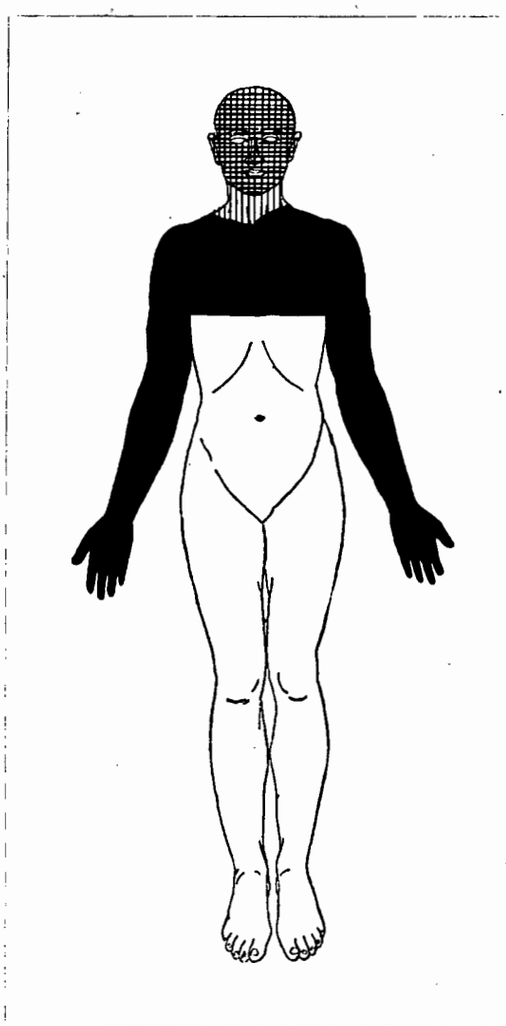


FIGURE 42.

Six months after removal of
Left Th.2, Th.3 and Th.4 and Right Th.2.

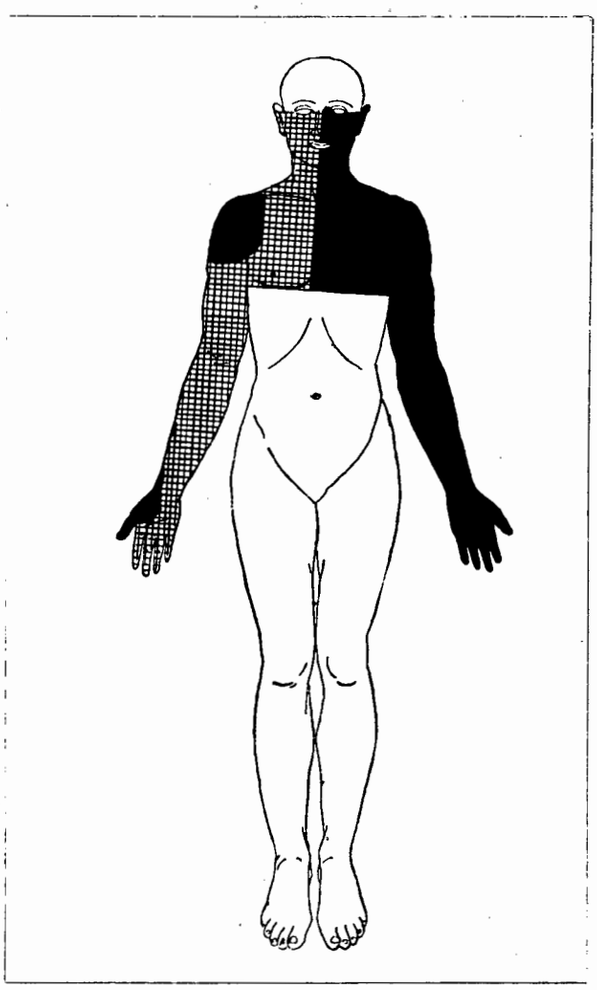


FIGURE 43.

Fourteen months after cauterisation of Left Th.2.

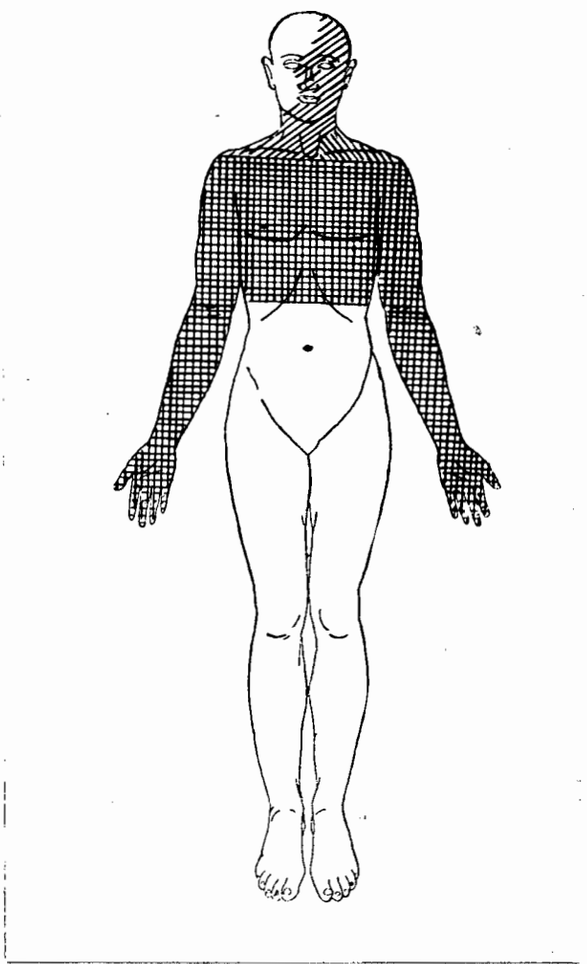


FIGURE 44.

Three years after bilateral cauterisation of Th.2.

Anterior Aspect.

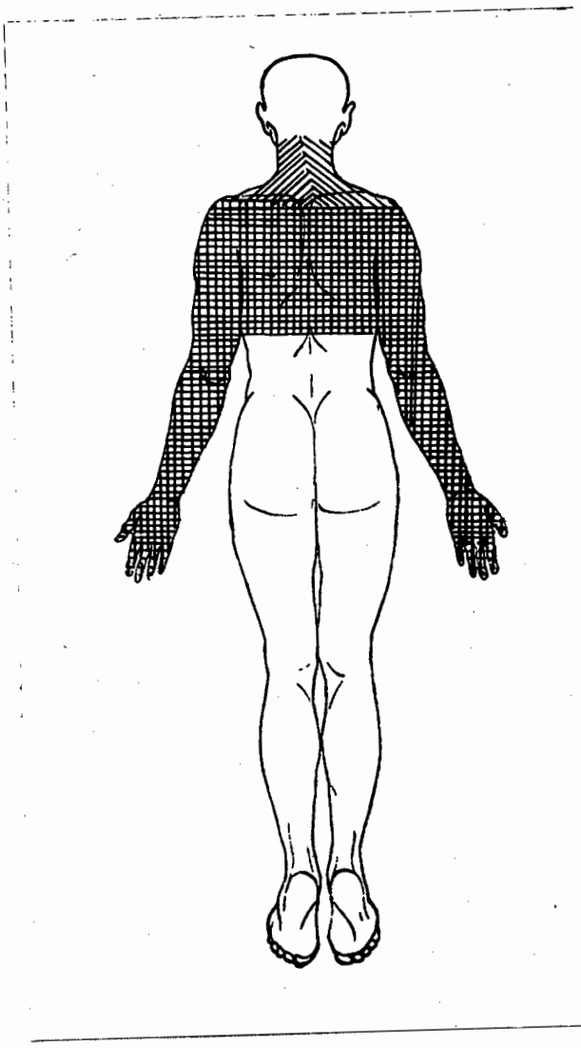


FIGURE 45.

Same case as in Figure 44.

Posterior Aspect.

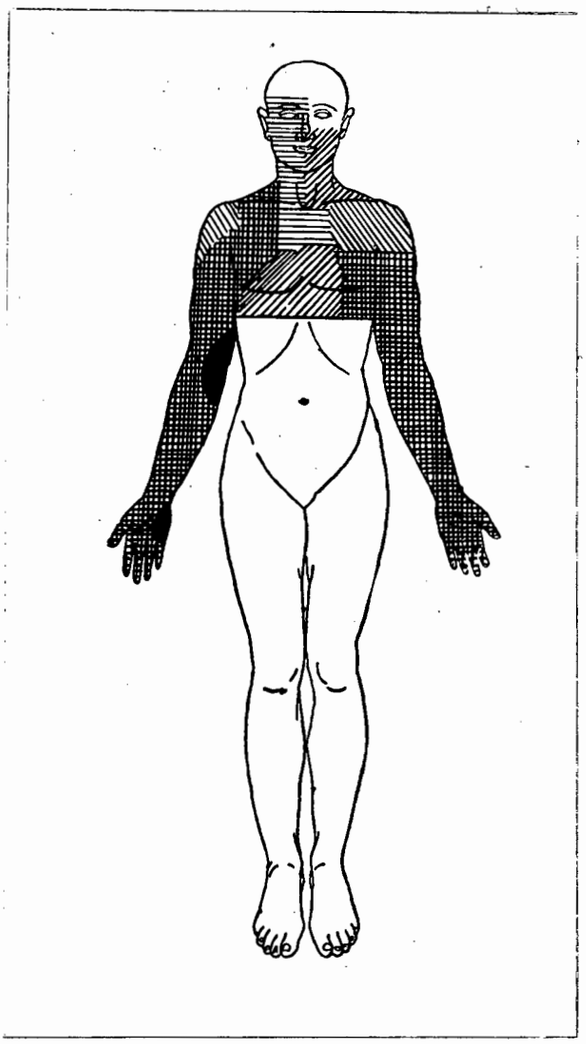


FIGURE 46.

Three years after bilateral cauterisation of Th.2.

Anterior Aspect.

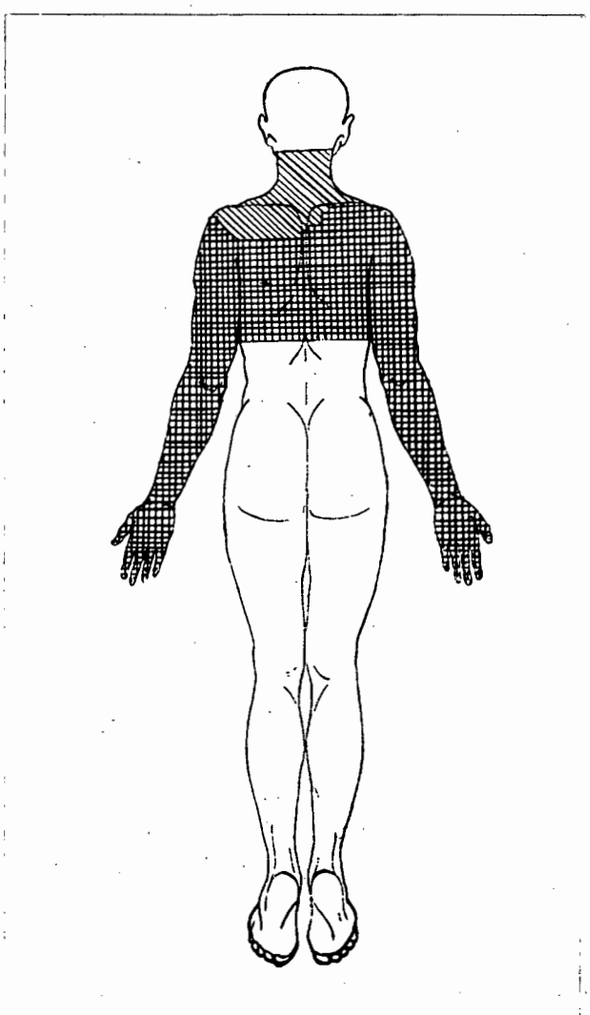


FIGURE 47.

Same case as in Figure 46.

Posterior Aspect.

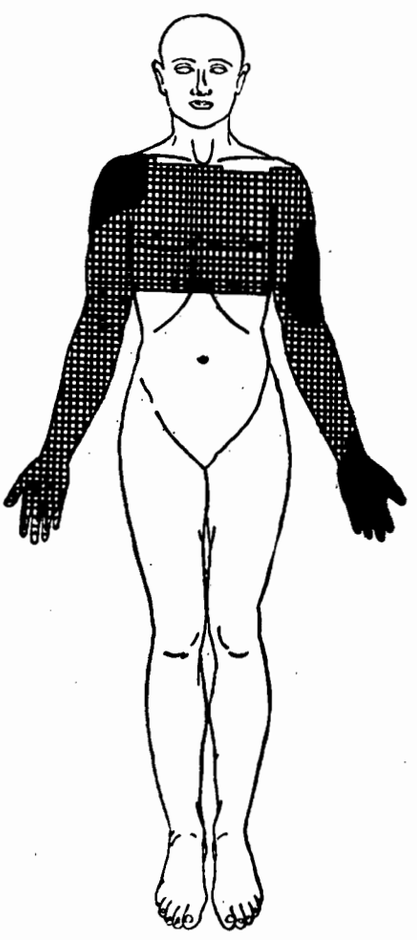


FIGURE 48.

Four years after cauterisation of Left Th.2.
and
removal of Right Th.2.

Anterior Aspect.

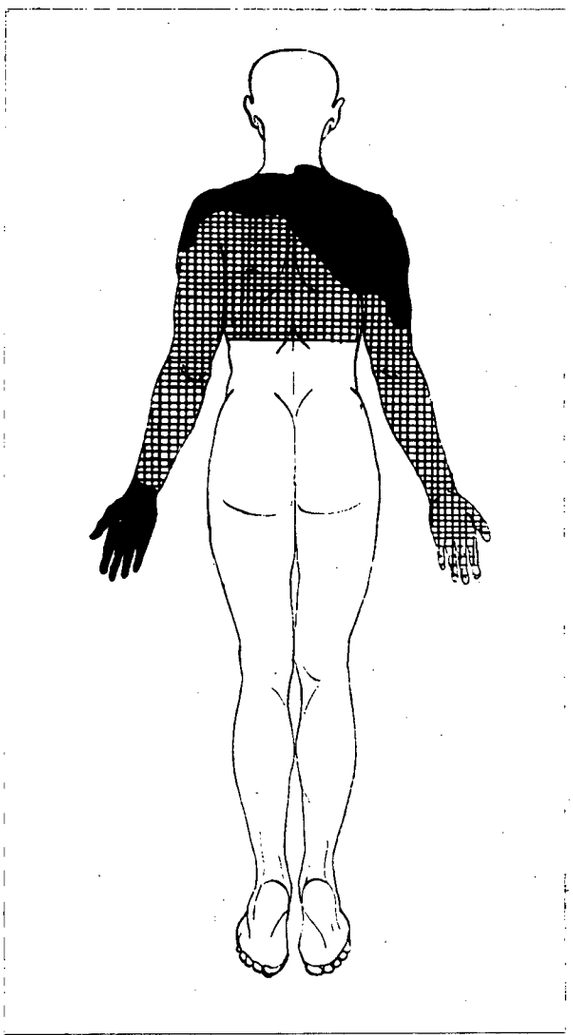


FIGURE 49.

Same case as in Figure 48.

Posterior Aspect.

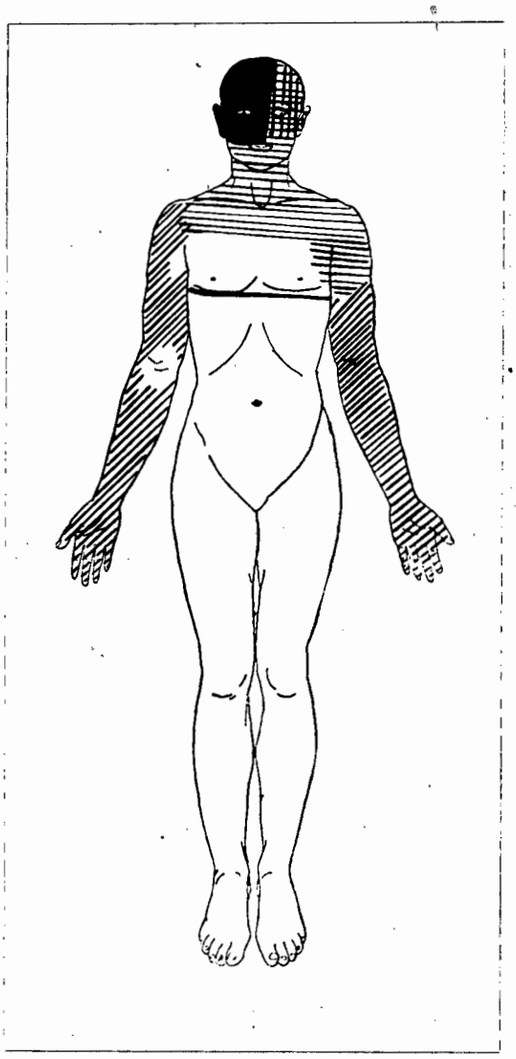
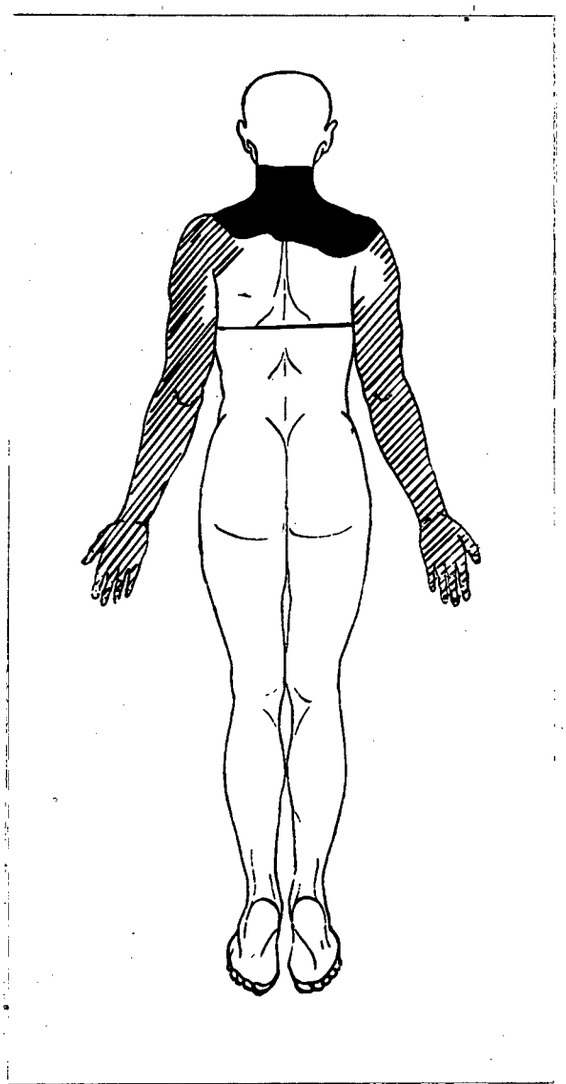


FIGURE 50.

Nine years after bilateral Telford's operation.

Anterior Aspect.



Right! Left!

FIGURE 51.

Same case as in Figure 50.

Posterior Aspect.

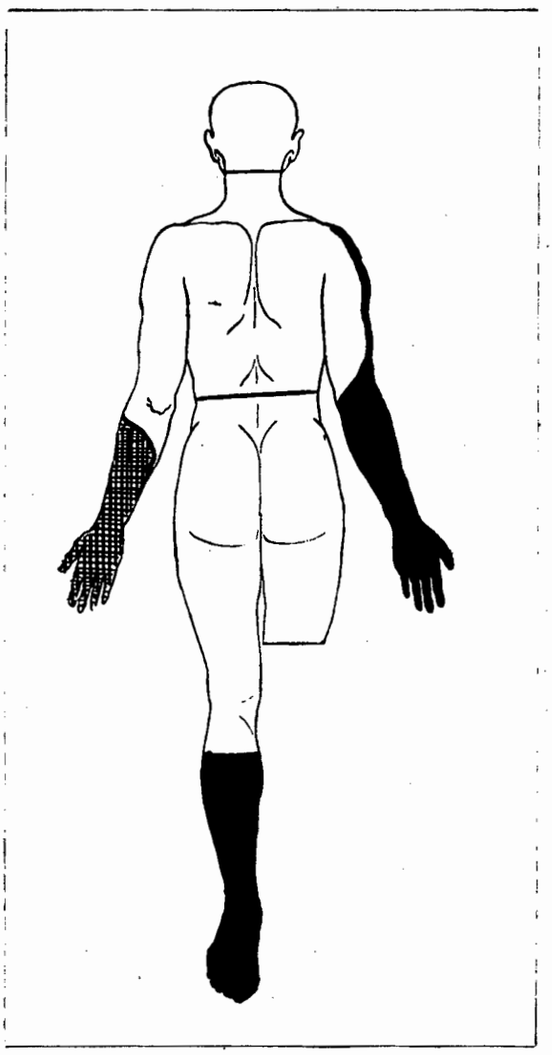


FIGURE 52.

Nine years after removal of
Right Stellate Ganglion.

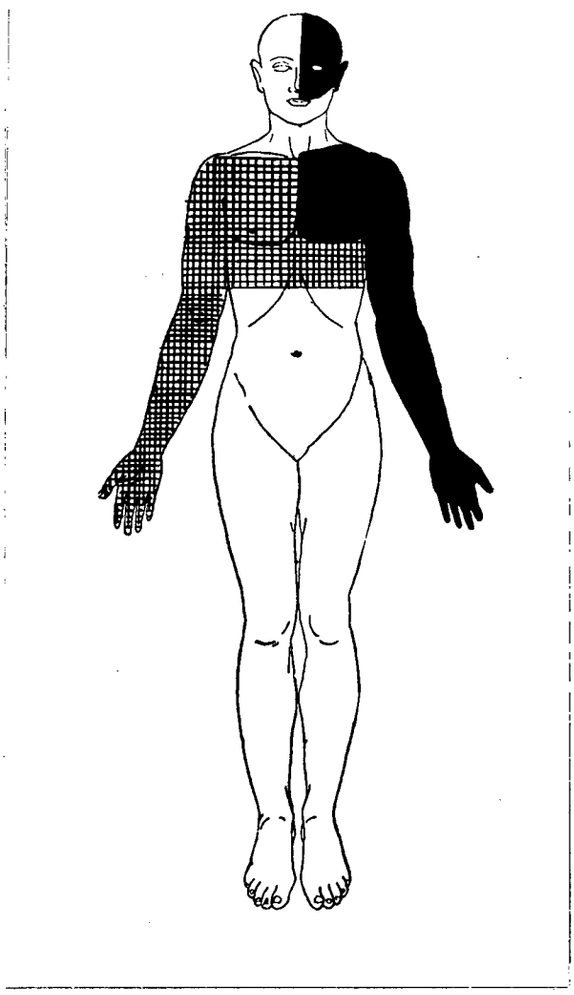


FIGURE 53.

Thirty years after removal of
Left Stellate and Second Thoracic Ganglia.

Discussion.

In assessing the value of the skin resistance test, as a means of determining the presence or absence of sympathetic innervation to the skin, the striking feature is the close similarity, in results of this test and the Minor Starch-Iodine sweating test. In all three types of patient examined, the patterns outlined are remarkably similar. Both tests, of course, are mainly dependent upon the reaction of the sweat glands.

All areas of high resistance, therefore, are considered sympathectomised. Any resistance of less than 500,000 Ohms implies intact sympathetic innervation to that area of skin. Areas of resistance of 100,000 - 500,000 cannot be accepted as areas of partial innervation. (Figure 53. - page 146). In this patient the areas of resistance of 100,000 - 500,000 are obviously normally innervated by the sympathetic system.

The result, therefore, indicates that those cases examined within six months of sympathectomy are still sympathectomised as judged by the skin resistance. That this is so, is particularly well shown by those patients with a unilateral sympathectomy. A striking feature is the manner in which the sympathectomised areas extend to the midline.

The late results, with one exception, show a marked patchiness in the areas of high resistance. In only one case, fourteen months after unilateral sympathectomy, was there evidence of uniform areas of high resistance. Here, too, the difference between the sympathectomised and the normally innervated sides was definite and well-marked. (Figure 43. - page 136).

The remaining patients all showed areas of low resistance predominantly. In isolated areas the resistance

/remained high

remained high but no connection between the areas was apparent in the group. This inconstancy of the pattern of areas of high resistance is a feature of these cases.

Therefore, the late results of sympathectomy of the upper extremities, by removal of the second thoracic ganglion only in patients suffering from Raynaud's Phenomena, show that sympathetic denervation is not as complete as the early results obtained by the skin resistance test. These results are in agreement with those obtained by the Starch-Iodine sweating test.

In those cases where sympathectomy had been performed for thrombo-angiitis obliterans and causalgia, the skin resistance shows that sympathetic denervation is still extensive nine and thirty years after operation respectively.

Those cases examined within six months of sympathectomy, all had the second, third and fourth thoracic ganglia removed. All the cases among the late results had had only the second thoracic ganglion removed. The non-Raynaud's patients had been sympathectomised by removal of the stellate ganglion alone or with the second thoracic ganglion.

3. Response to Pilocarpine.

Hyndman and Wolkin (1942) had observed that pilocarpine did not produce sweating in the extremity denervated by postganglionic section provided enough time had been allowed to elapse for degeneration of the postganglionic fibre to occur. Further, they observed that sweating occurred in the limb denervated by preganglionic section. In order to confirm this point, pilocarpine gr.1/6 was administered to a patient to induce sweating - preganglionic section had been done six months previously. Sweating occurred in the sympathectomised areas. Shortly after sweating had begun one hand was removed from the cover of the blankets to determine whether sweating

/was present

was present or not. After the hand had been exposed for a short while, Raynaud's Phenomena appeared. The hand was cold, blue and sweating!

The action of pilocarpine on the peripheral vessels was, therefore, studied in each of the cases examined in the series.

Further, pilocarpine was administered to six normal medical students to act as controls. None of these subjects had any suggestion of vascular abnormality. The sympathetic supply to the upper extremity in each case was intact.

Pilocarpine is the chief alkaloid from the leaves of Pilocarpus Jaborandi. The close similarity between pilocarpine and acetylcholine has been known for some time. Wilson (1934) commented on the similarity of the two drugs, on the haemodynamic responses and noted that the secretory responses are apparently identical. The similarity between pilocarpine and acetylcholine concerns the muscarine (smooth muscle and glands) and not the nicotine effects of the latter drug. Pilocarpine, however, is chemically distinct from acetylcholine. It does not inhibit cholinesterase and appears to act directly on effector cells.

Although Cushing (1931) suggested that pilocarpine, subcutaneously or intramuscularly, might act partly or wholly on a hypothalamic centre and not peripherally, Langley and Anderson (1904) had already established that sweating produced by pilocarpine occurred after division and degeneration of the secretory nerves. Further work by Langley (1922) and Burn (1922, 1925) confirmed this. They also demonstrated that the response to pilocarpine might occur, usually in greatly diminished amount, after division and degeneration of all nerves to the part. Adson and Brown, and Lewis have also observed that pilocarpine can induce sweating in a completely sympathectomised part.

/It was apparent

It was apparent that the autonomic responses to pilocarpine are due to a highly selective action of the alkaloid on cells innervated by postganglionic cholinergic fibres. The action is a direct one of the reactive substance and occurs after nerve section and complete nerve degeneration.

1. Normal Controls.

The same routine of administration and observation was adopted with the control subjects as with the patients examined. In all cases the subject reclined in a sitting position on the couch devised by Goetz. The body was covered by one blanket and only the hands, feet and face were exposed to the room temperature.

Continuous plethysmographic records were made of the fluctuations occurring in the digit examined. Regular blood pressure and skin temperature readings were taken throughout the duration of the test. The subject was asked to observe and remark on any departure from the normal.

In all cases the blood pressure and skin temperatures were observed for a period of at least fifteen minutes to allow for stabilisation.

Pilocarpine was then administered intramuscularly, usually into one or other deltoid muscle. 1/6gr. of the nitrate salt was given in all these cases. Some degree of discomfort was felt at the site of injection. The total quantity of fluid injected never exceeded 2.5cc.

The patient was closely observed. Should any distress or discomfort have resulted, atropine was administered. 0.5mgm. was given intravenously if a suitable vein was found. If no suitable vein presented, the atropine was given subcutaneously without any attempt to administer the drug intravenously.

/Pilocarpine

Pilocarpine is absorbed fairly rapidly and the first effect of the drug may become apparent within a minute. In some, however, the first effects were noted ten minutes later.

A feeling of warmth in the face is usually the first effect noted by the subject. The face may actually appear flushed. This "flushing" is felt over the whole face and also the anterior part of the sternum. Four of the six control subjects were conscious of this sensation. The time of onset varied from one to ten minutes after injection. Flushing was the earliest effect of pilocarpine noticed. It preceded salivation in every case in which it occurred. The total duration of this sensation varied from three to eleven minutes and in all cases was of shorter duration than the duration of salivation.

Salivation was a constant feature in all cases. The quantity of saliva produced, although never estimated, varied according to each individual. The increased secretion of saliva began 1 to 10 minutes after pilocarpine administration. It was usually preceded by the flushing of the face, but in one case salivation preceded flushing. Increased flow of saliva lasted about twenty minutes or until a minute or two after the injection of atropine. Atropine given intravenously caused cessation of salivation sooner than intramuscular administration.

Increased nasal secretion was manifest in two out of the six control subjects studied. It became apparent shortly after salivation had started and lasted for a similar period.

In none of the control subjects studied was evidence of increased bronchial secretion present.

Nausea was present in one of the control subjects, but was only a transitory phenomenon.

One subject noticed blurring of vision. At this stage dilatation of the pupils was present.

/Sweating

Sweating was present in all the subjects examined. The first sign of sweating usually became manifest on the forehead and face. It began 7 to 22 minutes after injection, and always occurred well after the onset of salivation. Sweating then rapidly occurred on the covered parts of the body, and finally was perceptible on the exposed hands. In none of the cases examined was sweating noted on the dorsum of the feet, although the plantar surfaces and the lower leg sweated.

Sweating persisted for about twenty minutes. If atropine was given, sweating perceptibly ceased 5 to 10 minutes after administration.

Cutis anserina was observed in one subject. It was accompanied by a sensation of tingling in the forearm. The hair was visibly erect on inspection. This feature, however, was not observed in all subjects.

The following factors were noted by continuous plethysmographic tracing throughout the duration of the test:-

(1) Pulse rate:-

The resting pulse rate before the administration of pilocarpine was 70 to 90 beats per minute in all six subjects. Fluctuation naturally occurred according to the individual, but, nevertheless, the variation was never great.

In three of the six subjects the actual intramuscular injection had little or no effect on the pulse rate. In two subjects a rise in rate of 20 beats per minute occurred simultaneous with the injection. In the remaining subject the rate increased from 90 to 126 beats per minute on injection.

No slowing was observed in any subject following pilocarpine administration. In five out of six subjects, the rate increased 10 to 15 beats per minute. This increase in rate was maintained until the completion of the test or until atropine was given. In one subject pilocarpine had little or

/no effect

no effect on the rate of the heart.

(2) Pulse volume:-

The effect of pilocarpine on the volume of the pulse is difficult to assess in the normal non-sympathectomised individual. Factors such as excitement, anxiousness, breathing, etc. are impossible to avoid. Even the pulse volume at rest, before the administration of the drug, is subject to considerable fluctuation.

Nevertheless, the pulse volume in four of the six subjects showed an appreciable decrease. In one subject the pulse volume (apart from minor fluctuations) did not diminish after injection. In the remaining subject an actual increase in pulse volume was apparent.

An increase in pulse volume lasting 5 to 15 minutes was apparent in three subjects. Thereafter the volume decreased steadily. The increase in pulse volume occurred in all cases, where present, before sweating became clinically perceptible. In those cases where constriction occurred, i.e. decrease in pulse volume, sweating was already established. In the one subject that received pilocarpine only, the pulse volume showed a tendency to rise when sweating had ceased. Cessation of sweating as produced by atropine, did not result in an increase of pulse volume in four subjects.

(3) Digital volume:-

As would be expected the fluctuation in the volume of the digit, enclosed in the plethysmograph tube, is dependent on the rate of the pulse and on the height of the pulse volume. Variations in either of these factors will influence the digital volume.

In the normal non-sympathectomised digit, reflex and other phenomena greatly influence the volume of the digit at rest. Thus stabilisation of the volume is not an easy matter. Other criteria - skin temperature and blood pressure, were used to determine whether the digital volume was

/stationary

stationary before administration of pilocarpine.

Even though the skin temperature and blood pressure may have attained a constant course, considerable variation in the pulse and digital volume may still occur.

In three subjects a slight rise in the volume of the digit occurred within a few minutes of administration of pilocarpine; the increase in digital volume, however, was not very great, the average rise being 0.1cc. Subsequent studies show that the rise is only transient and a decrease eventually ensues.

Five subjects showed a decrease in digital volume, with or without a preliminary increase. In the remaining subject there was no initial effect at all of pilocarpine. In the latter subject fifteen minutes after injection, the volume of the digit gradually increased 0.7cc. This increase in digital volume was maintained after atropine was administered, a further rise of 0.5cc. being encountered.

The decrease in digital volume varied from 0.3cc. to 1.0cc. in the subjects tested. In all cases the decrease in digital volume was associated with a fall in pulse volume and in skin temperature.

It is further of note that the fall in digital volume occurred at or about the time of onset of sweating. It would thus appear likely that the fall in digital volume in these subjects is directly related to the evaporation of sweat from the exposed surfaces.

In the sixth subject no decrease in digital volume occurred. In this person both arms were completely covered by blankets, only the hands and face being exposed. It is likely that, although sweating occurred as easily and as readily as in the remaining subjects, evaporation and consequent cooling did not take place. This lends further

/support

support to the fact that vasoconstriction, as produced by pilocarpine in normal subjects, is not due to the direct action of the drug on the vessels, but results from the cooling ensuing on sweating, produced by pilocarpine.

In one subject the response of the digital volume to pilocarpine only was noted. Sweating appeared to stop spontaneously thirty-one minutes after administration of the drug. At this point, or shortly after, the digital volume began to rise and was still increasing at the end of the test.

All the remaining subjects were given atropine to terminate the secretory effects of pilocarpine. The digital volume in one subject, after an initial fall of 0.6cc. immediately following intravenous administration, increased 1.4cc. during the next fifty minutes. In one subject a rise in digital volume occurred after administration of atropine. The increase in digital volume became apparent in both subjects after the cessation of sweating. In the remaining two subjects cessation of sweating, by the administration of atropine, did not appear to influence the digital volume.

In spite of the two subjects in which no rise in digital volume occurred after cessation of sweating as induced by atropine, the hypothesis postulated above, viz. that pilocarpine does not cause vasoconstriction by direct action on the vessels, is confirmed.

The constricting action of pilocarpine is apparently due to the local cooling effect of the evaporation of sweat, induced by the drug.

(4) Skin temperature:-

In five subjects skin temperature readings showed very little variation before the administration of pilocarpine. In the remaining subject considerable fluctuation was present.

/The skin temperatures

The skin temperature of both middle fingers rose 8 - 9°C. and again decreased 3 - 4°C. before the drug was given. The temperature was falling when pilocarpine was injected.

In all six subjects examined, a fall in skin temperature occurred after injection of pilocarpine intramuscularly. A gradual drop took place in all cases. The decline started in 5 to 15 minutes and occurred before sweating and salivation became clinically perceptible. The decline varied from 2 - 5°C, and was maintained in all, except one. In this subject, after an initial fall of 2 - 3°C., the temperature began to rise seventeen minutes after pilocarpine administration. At this stage salivation was marked, but increased sweating had not yet become clinically noticeable. No rise in skin temperature was apparent in any of the subjects examined.

In the one subject that received pilocarpine only, a rise of 3°C. occurred 30 to 40 minutes after injection. At this point sweating and salivation had ceased.

Atropine did not appreciably affect the decline of the skin temperatures. In three subjects a further slight fall occurred and although the secretory effect of pilocarpine had ceased, no increase in skin temperature occurred.

One subject showed a further decline of 1°C. after atropine injection, but three minutes later, i.e. more than twenty minutes after the cessation of all the secretory effects of pilocarpine, a rise in skin temperature became manifest.

In the remaining subject atropine was administered while the skin temperature was still rising. A further rise of 2 - 4°C. occurred.

/Pilocarpine

Pilocarpine, thus, produces a fall in skin temperature in the normal non-sympathectomised digit. This fall becomes manifest a short while before sweating, resulting from the drug, is clinically perceptible. Following the cessation of sweating, whether induced by atropine or not, the skin temperature may decline further or may increase. It appears likely that any further decline would be due to continued evaporation of sweat still present on the exposed hands.

(5) Blood Pressure:-

There appeared to be a fairly constant level of both diastolic and systolic pressures in each of the six subjects before the administration of pilocarpine. As a group the systolic pressure varied between 105 and 160 mm. Hg. The diastolic pressures were more consistent, the maximum variation never exceeding 10mm. Hg. The diastolic pressures registered varied between 65 and 90mm. Hg.

In the one subject where pilocarpine only was administered, a rise of 30mm. Hg. in systolic pressure occurred at the time of injection. This rise was maintained for ten minutes, subsequent to which a further rise of 10mm. Hg. occurred in the next fifteen minutes. Little effect was observed in the diastolic pressure until twenty minutes after injection. Apart from a single reading, 10mm. Hg. lower than the resting diastolic pressure, a slow and gradual rise of 5 to 8mm. Hg. occurred. Twenty-five minutes after injection, the diastolic pressure rose a further 15mm. Hg. The pressure was maintained at, or slightly below, this higher level until the completion of the test. A gradual decline in systolic pressure had meanwhile occurred.

In this subject the rise in systolic pressure occurred before sweating became perceptible clinically, although salivation was already established. The rise in diastolic pressure

/apparently

apparently only occurred when sweating was firmly established. The gradual decline of both systolic and diastolic pressures appears to coincide with cessation of sweating.

The changes in the remaining five subjects are not very marked. Little or no decrease in systolic pressure occurred. One subject had a rise of 15mm. Hg. after injection. Apart from this, the systolic pressures, at the moment of administration of atropine, were approximately the same as the resting levels.

Similarly, the effect of pilocarpine on the diastolic pressure in these subjects was minimal. If anything, the diastolic pressure appeared to be slightly lower than the resting levels.

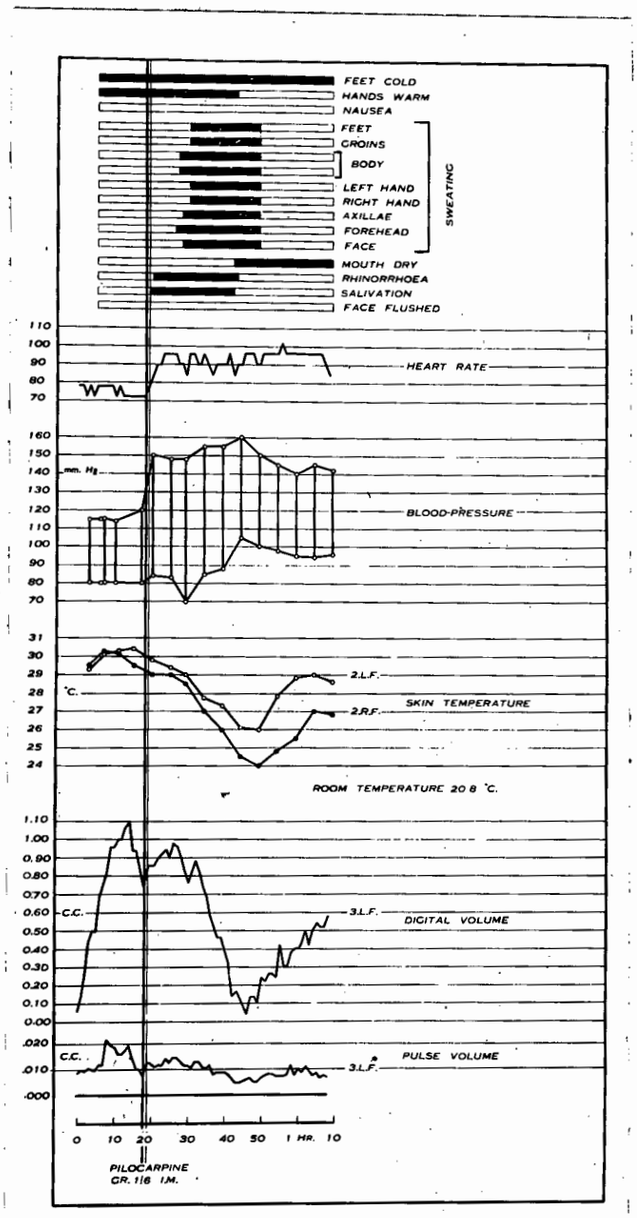
In all these subjects the secretory effects of pilocarpine were well established.

Atropine, however, had a marked effect on the blood pressure, as well as causing an abrupt cessation of the secretory effects of pilocarpine. The diastolic pressure mainly was effected. A rise took place within a minute or two of intravenous administration. This rise in diastolic pressure took place in all subjects and varied between 10 and 50mm. Hg. At the same time there was a tendency for the systolic pressure to decrease. A small rise occurred at the moment of injection but the general effect was to diminish the systolic pressure.

In one subject the effect of atropine was rather striking. Within four minutes the systolic pressure rose from 120mm. Hg. to 180mm. Hg. and the diastolic from 70mm. Hg. to 120mm. Hg. At this point the subject noticed palpitations and some praecordial discomfort. This startling effect rapidly subsided, the systolic pressure quickly dropped to 150mm. Hg. although the diastolic pressure only settled at 110mm. Hg.

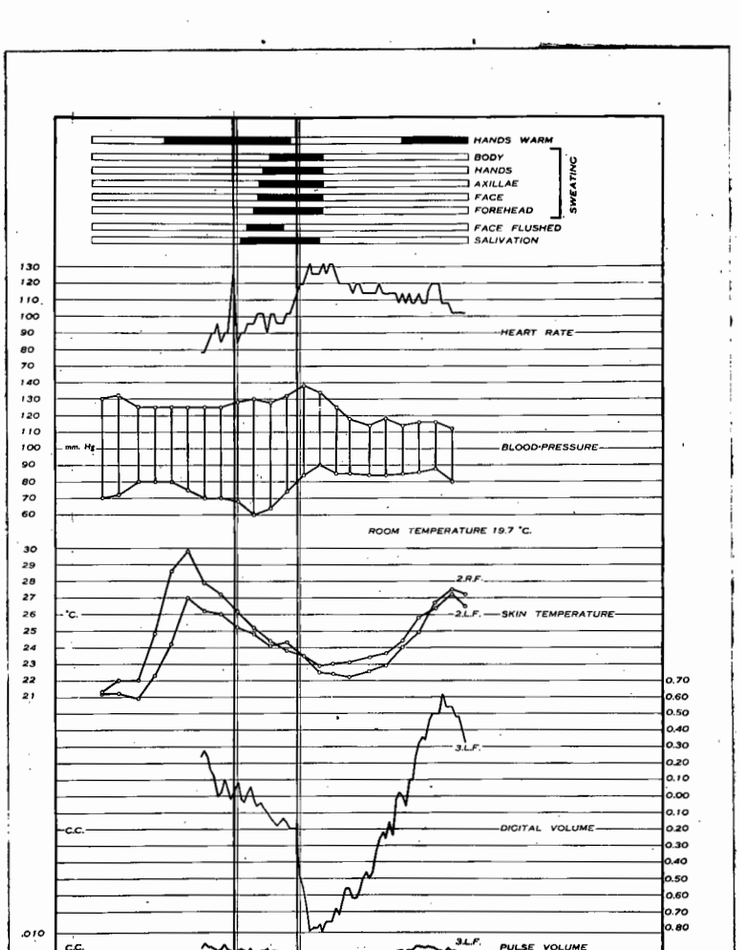
The sum total of the effect of atropine was a diminution in pulse pressure. This feature was common to all the subjects examined.

The effect of pilocarpine on the normal non-sympathectomised extremities is shown graphically hereunder:



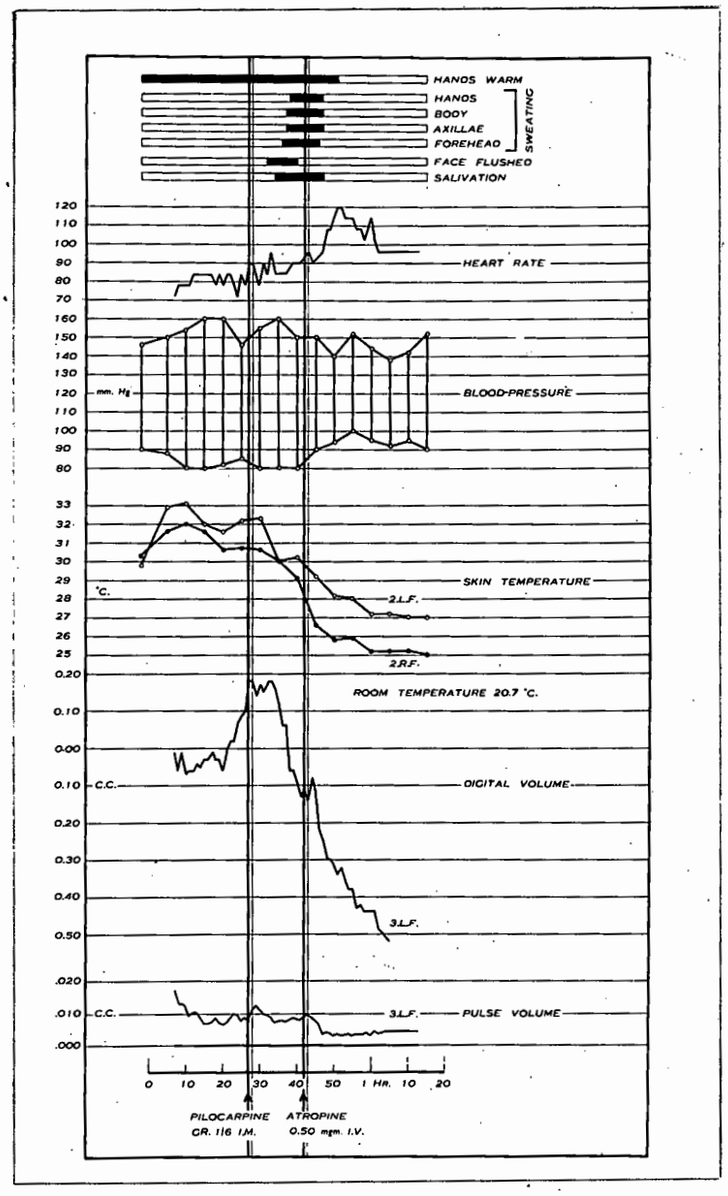
GRAPH 1.

Normal Control No. 1.



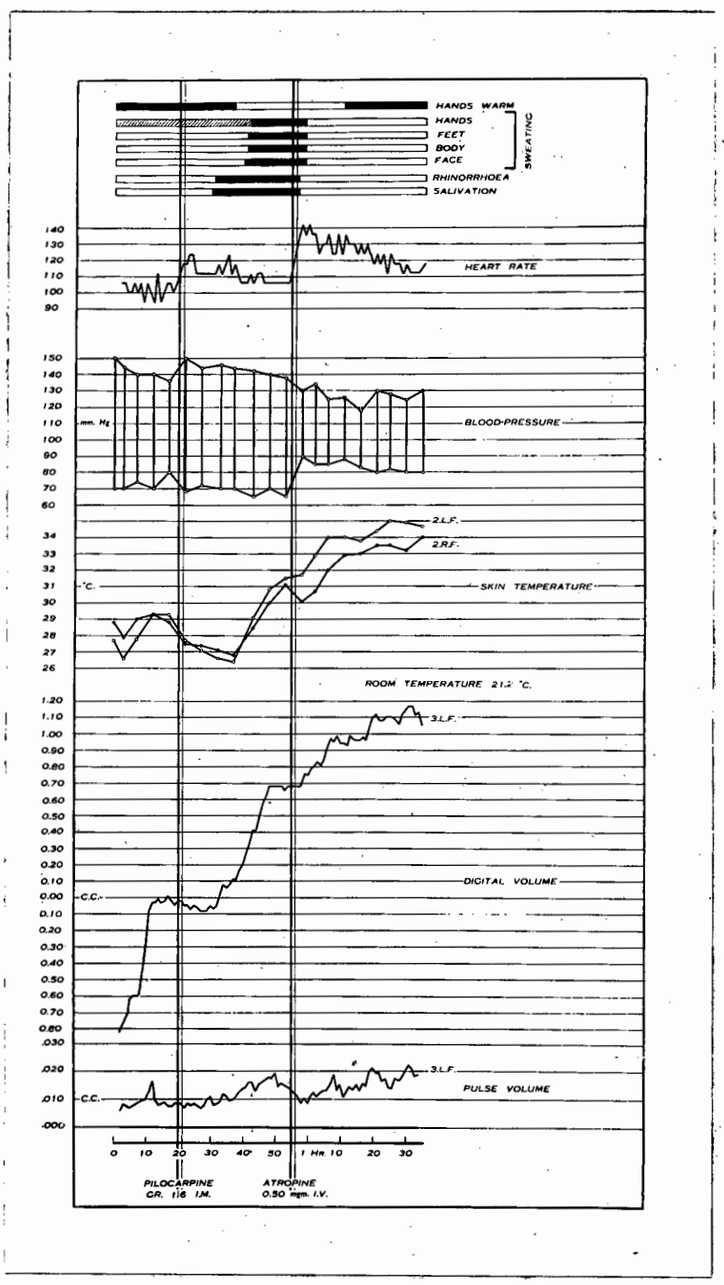
GRAPH 2.

Normal Control No. 2.



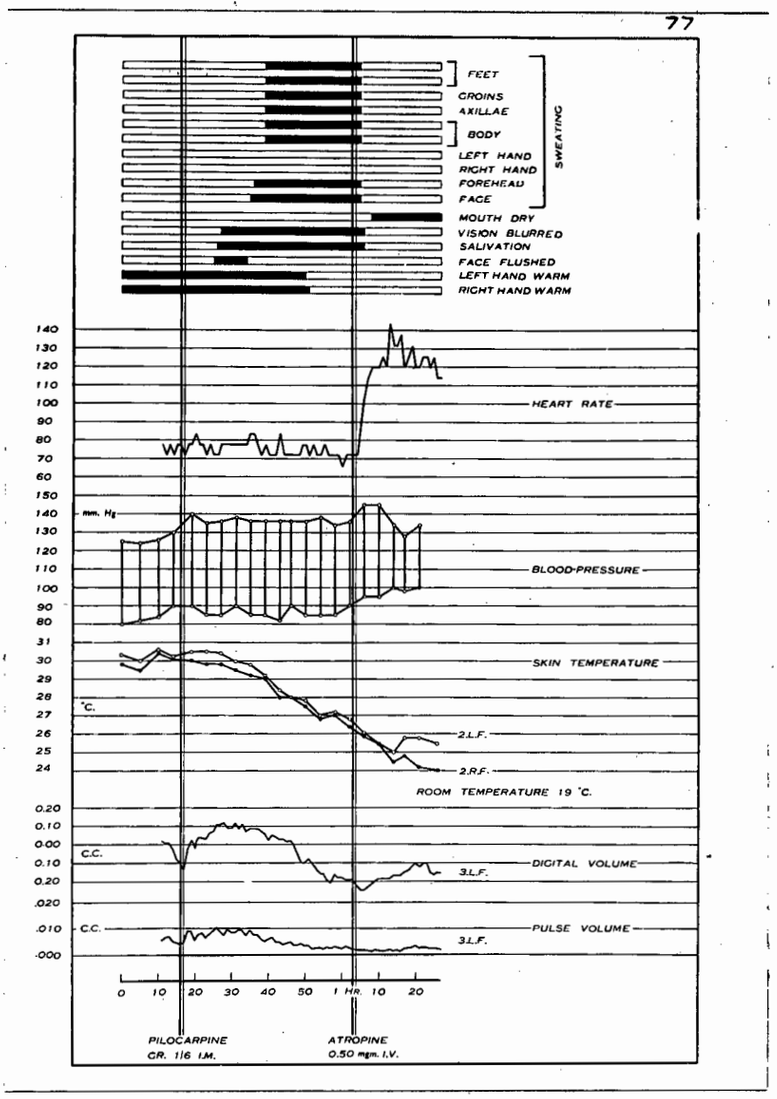
GRAPH 3.

Normal Control No. 3.



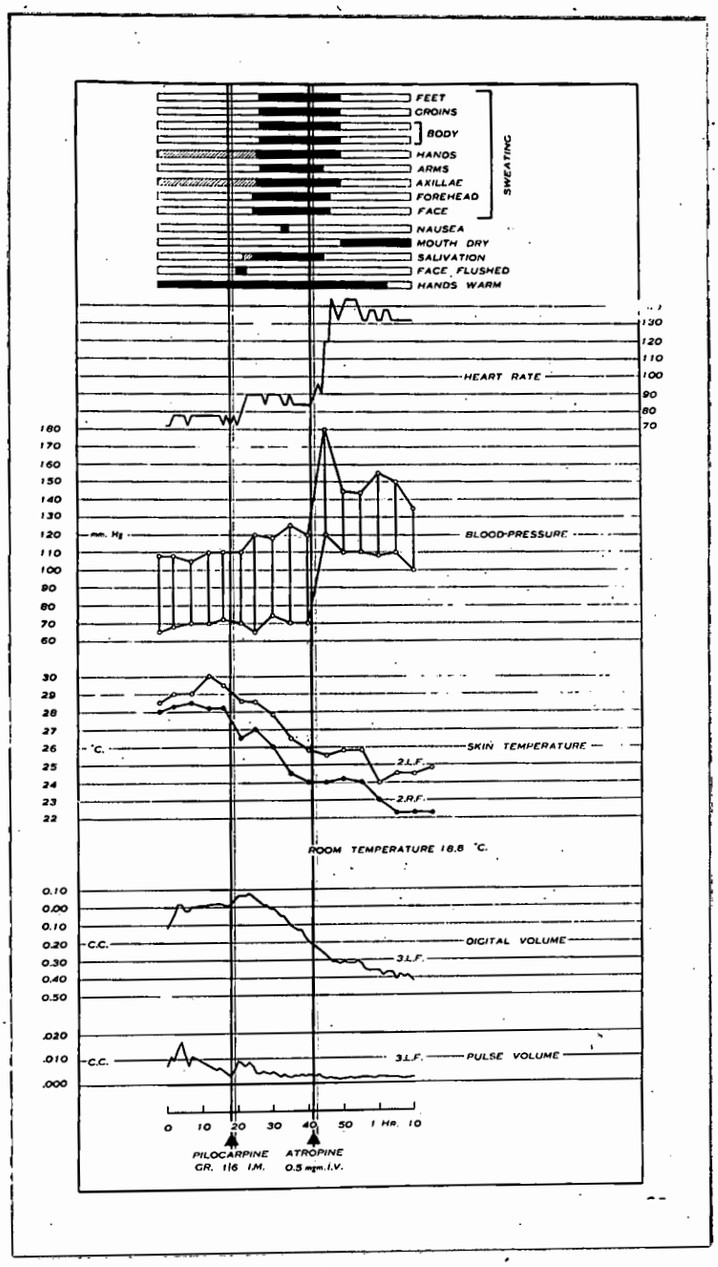
GRAPH 4.

Normal Control No. 4.



GRAPH 5.

Normal Control No. 5.



GRAPH 6.

Normal Control No. 6.

11. Raynaud's Phenomena.

The effect of administering pilocarpine to patients with Raynaud's Phenomena was observed in three instances. The reaction of the normally innervated upper extremity to the drug is apparently that of vasoconstriction. During Raynaud's Phenomena the vessels are constricted and these cases were tested to determine whether any further vasoconstriction will occur. Thus, it was possible to observe one case before any operative procedure had been undertaken and also two cases where unilateral sympathectomy had been performed. Any difference between the normally innervated extremity and the extremity of Raynaud's Phenomena was observed. Also the difference in Raynaud's Phenomena before and after sympathectomy was noted.

Graph 7. (page 171) depicts the result of administration of pilocarpine gr. 1/6 intramuscularly before any operative procedure had been undertaken on either side, in a case of Raynaud's Phenomena. The patient was observed for twenty minutes before the drug was given. During this period it was rather difficult to find a stable level of skin temperature of either hand in order to standardise observations.

Both hands were cold and blue and just reached room temperature. No sweating was apparent anywhere. After twenty minutes the skin temperature had risen slightly to 21°C. and 19°C. on the right and left hands respectively. Pilocarpine was administered at this point. The rise in temperature was maintained for a further eight minutes. Subsequent to this a gradual decline occurred, the temperature of both middle fingers finally settling at 19°C. and 21°C.

The pulse volume of the right middle finger shows

/a steady

a steady line at about 0.005cc. with a sudden peak just before the injection. At the time of injection, however, the pulse volume had returned to the previous level. At first, little effect was noted but, as the graph indicates, a gradual decrease occurred and at the conclusion of the test, the pulse volume was 0.002cc., i.e. even lower than at the outset.

The digital volume shows changes very similar to the skin temperature. The volume rises slowly to the moment of injection. After injection there is a momentary decrease followed by the maintenance of the volume at a slightly higher level. There is then a gradual decline to slightly above the resting level.

The effect on the blood pressure is not very great. The diastolic level did not vary but the systolic pressure rose 10 - 20mm. Hg.

A slight increase in heart rate occurred.

Subjectively, the face felt flushed within six minutes of injection. Salivation became obvious three minutes later. Sweating first became apparent on the face ten minutes after injection and in the axillae two minutes later. Sweating was not very gross on the exposed hands but, nevertheless, occurred.

It is worthy of note that the decrease in skin temperature, pulse volume and digital volume was not really apparent until the secretory effects of pilocarpine had been well established.

Graph 3. (page 172) shows the effect of pilocarpine on a normal, i.e. non-sympathectomised, upper limb twelve days after the opposite extremity had been sympathectomised. This patient, too, had Raynaud's Phenomena.

/As judged by

As judged by the skin temperature of the non-sympathectomised extremity, the vessels were fully dilated. Little variation in temperature occurred before administration of the drug. After gr.1/6 had been given intramuscularly a slight rise became apparent. The rise was, however, not great. Twenty minutes after administration the temperature started decreasing. The fall was fairly rapid and at the termination of the test the temperature was 27°C. (at the outset 32 - 33°C.).

The pulse volume fluctuates considerably before the injection. A fall of very nearly 0.01cc. occurred at the moment of injection. The volume, however, quickly recovered. A further dilatation occurred after injection. The maximum volume was 0.048cc. Fourteen minutes later a rapid decline occurred and thirty minutes later the pulse volume of the digit was 0.002cc.

The marked change in pulse volume is reflected on the digital volume. There was no increase in digital volume immediately after injection. For nearly twenty minutes the volume of the digit was maintained. In the next thirty minutes, however, the decrease in digital volume was nearly 2cc.

There was an increase in heart rate from 100 to 120 beats per minute.

Again, the secretory effects of pilocarpine were well established before the constrictor effect occurred.

A similar picture is seen in Graph 9. (page 173). Here, too, a patient with Raynaud's Phenomena had undergone sympathectomy of the other side, but on this occasion seven days previously.

The skin temperature of the normally innervated digit from an even steady 30°C. dropped to 26°C. in the fifty minutes subsequent to injection.

/The average

The average resting pulse volume was 0.006cc. Ten minutes after injection the maximum level of 0.01cc. was reached. This was succeeded by a gradual decline to 0.003cc. forty-five minutes after administration.

The digital volume continued to increase gradually after administration, but decreased slowly twenty minutes later to be slightly below the resting volume observed initially.

The secretory effects of pilocarpine were fully established before the constrictor effects began.

By contrast, another patient had been sympathectomised for causalgia thirty years previously. Pilocarpine by intramuscular injection had no effect on the skin temperature of the non-sympathectomised extremity. (Graph. 10 - page 174). No decrease occurred nor was there any appreciable increase.

The pulse volume of the non-sympathectomised extremity showed considerable fluctuation even at rest. The average resting level was 0.025cc. At the moment of injection there was a marked fall in pulse volume to 0.01cc. Recovery was immediate to 0.035cc. Thereafter a gradual tendency to decrease can be seen. The average volume fifty minutes after injection was 0.02cc: a slight, but definite decrease from the resting level.

The digital volume did not vary very much in response to pilocarpine. Nevertheless, a definite tendency towards constriction is noticeable particularly at the termination of the test.

The secretory effects of pilocarpine occurred as usual on the non-sympathectomised side. The onset of these effects, however, took place some while later than usual. It was only when the secretory effects had been established that the tendency to vasoconstriction ensued.

/Conclusions:-

Conclusions:

The effect of intramuscular injection of pilocarpine gr.1/6 was observed in ten individuals with intact sympathetic innervation to an upper extremity. The following facts were observed:-

(1) Secretory effects occurred in all. The time of onset varied in each case, but occurred within 1 to 15 minutes.

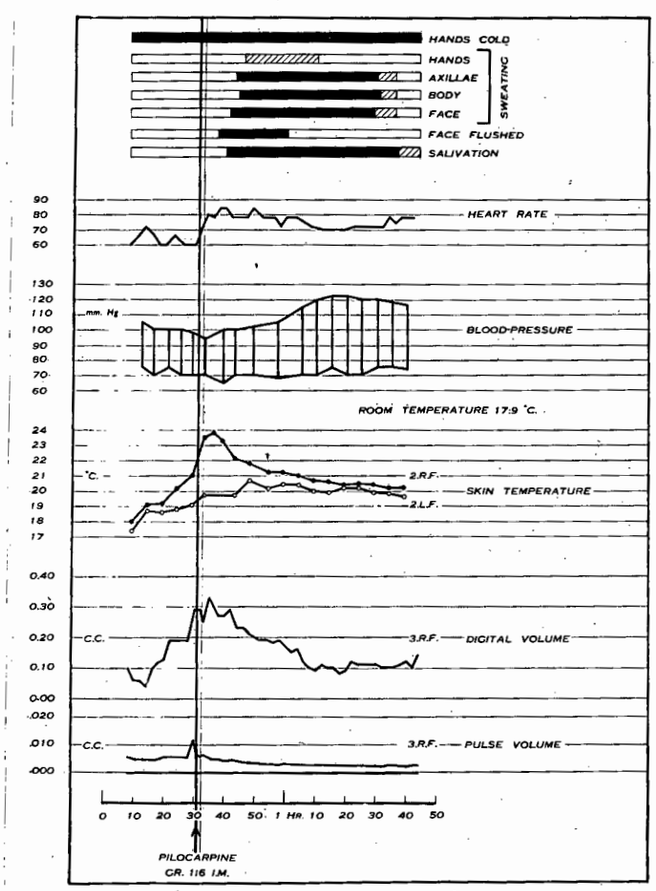
(2) Plethysmographically dilatation of the digital vessels was not observed in normally innervated extremities.

(3) Constriction of the digital vessels results after the injection of pilocarpine.

(4) This vasoconstriction does not appear to be due to the direct action of the drug on the vessels.

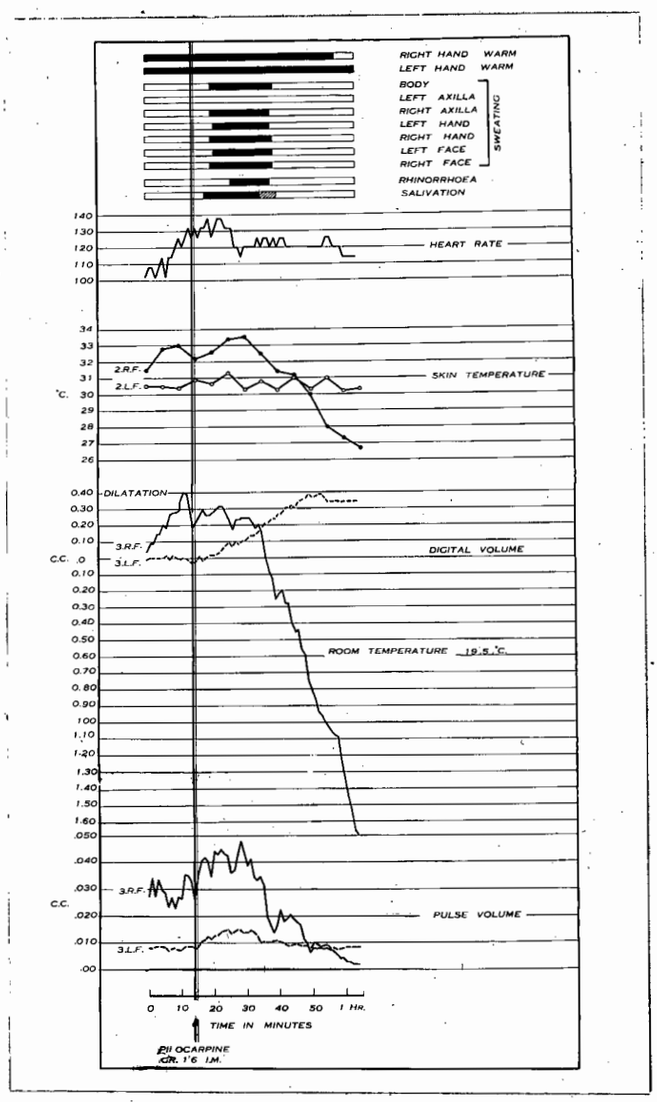
(5) It became established only after the secretory effects were clinically manifest. It is, therefore, likely that vasoconstriction, as induced by pilocarpine, is due to the local action of the vessels secondary to the cooling resulting from the evaporation of sweat from the extremities.

(6) There is no apparent difference in the reaction to pilocarpine of the normal extremity and the extremity of Raynaud's Phenomena. In the latter the secretory effects occur as usual; vasoconstriction occurs at relatively the same time; the degree of vasoconstriction is less because of the small pulse volume at rest; and the extremity is unable to constrict much more as the vessel is already in spasm.



GRAPH 7.

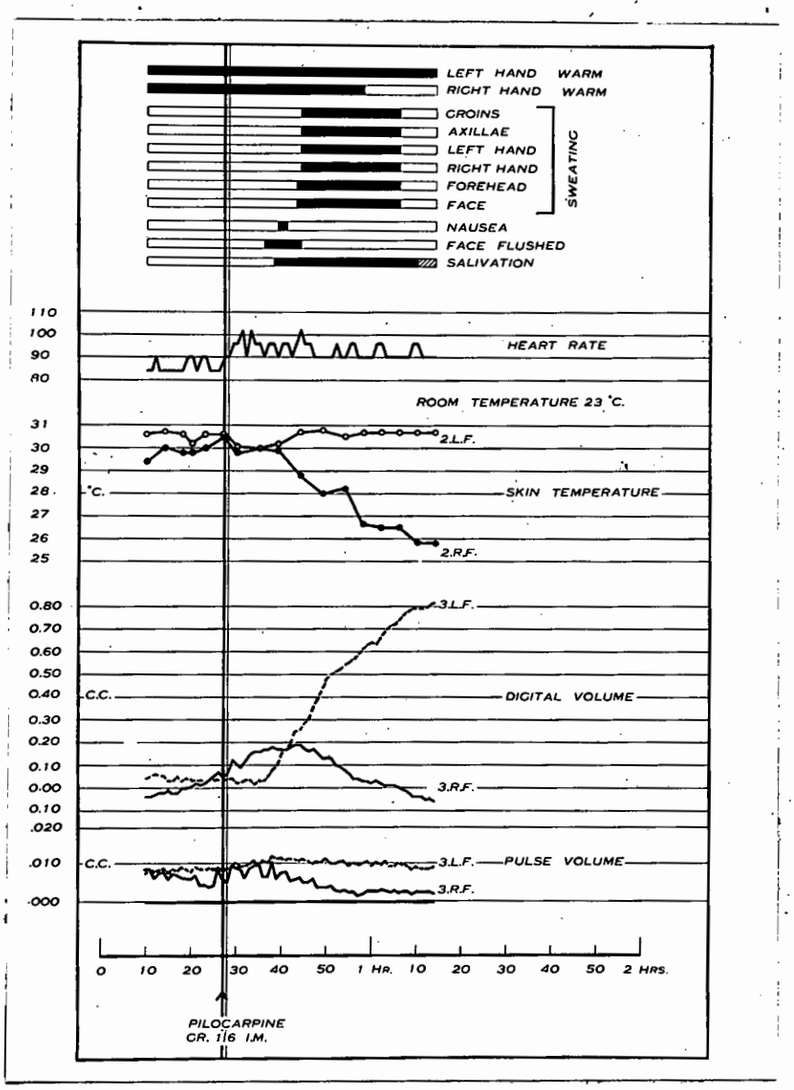
The effect of pilocarpine
on a patient with Raynaud's Phenomena
before any operative procedure.



GRAPH 8.

The effect of pilocarpine on a patient with Raynaud's Phenomena.

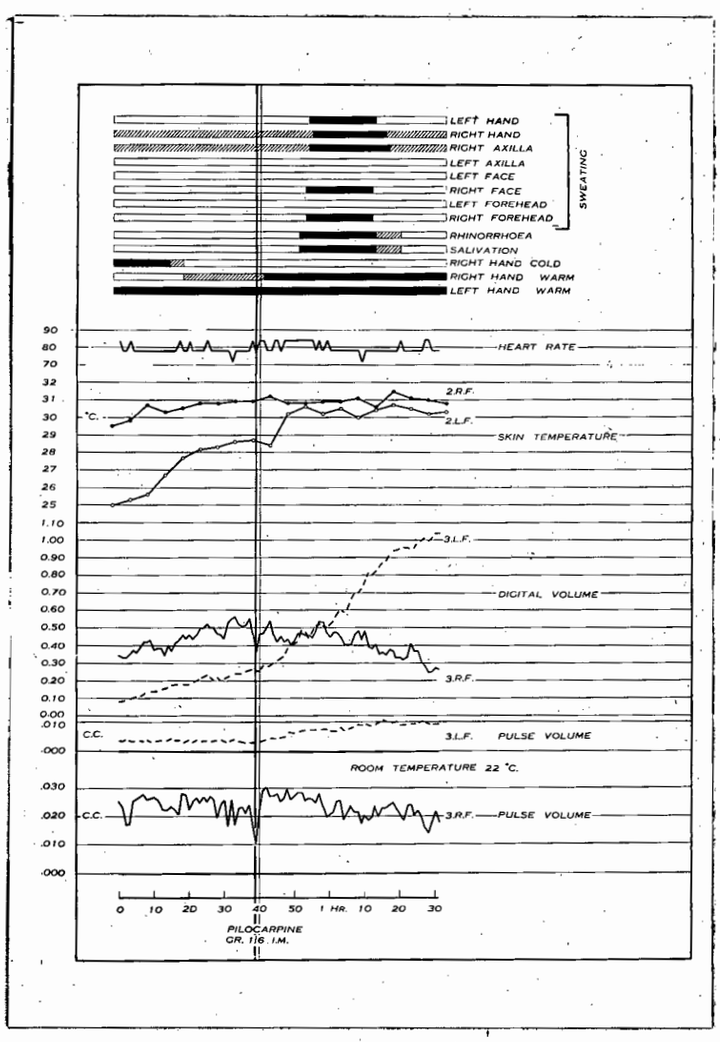
Left Th.2, Th.3 and Th.4 removed twelve days previously.



GRAPH 9.

The effect of pilocarpine
on a patient with Raynaud's Phenomena.

Left Th.2, Th.3 and Th.4 cauterised seven days previously.



GRAPH 10.

The effect of pilocarpine
thirty years after removal of
Left Stellate and Second Thoracic Ganglia

The effect on the normal extremity is also shown.

iii. After Sympathectomy.

Pilocarpine was administered to all patients who had been sympathectomised. The type of sympathectomy varied in many of the cases examined and also the duration after sympathectomy varied considerably.

Thus the second thoracic ganglion only was removed or cauterised in eight subjects. However, only thirteen upper extremities had been sympathectomised in this manner. Both the second and third thoracic ganglia were removed in two subjects, constituting four such sympathectomies. The second, third and fourth thoracic ganglia were removed in six subjects. A total of eleven sympathectomies are available in this group. Lastly the stellate ganglion was removed in one subject and the stellate and second thoracic ganglia were removed in another.

The cases were studied as early as the eighth post-operative day. In three cases the records were first observed within twenty-one days of operation. Two cases were observed three months after sympathectomy and two within eight months. Six subjects were re-examined 2 to 4 years after sympathectomy and two nine years later. One case was observed in which sympathectomy had been performed thirty years ago.

It is proposed to deal with the cases firstly with regard to duration after sympathectomy:-

(1) Immediate post-operative period.

Five patients were observed within this period. In each of these cases the second, third and fourth thoracic ganglia were removed. Sympathectomy was carried out by removal of the ganglia and intervening chain in two patients and by endothoracic cauterisation in the remaining subjects.

/All three

All three sympathectomised extremities were noted to be warm and dry and no Raynaud's Phenomena had been observed since operation. No sweating had taken place. The non-sympathectomised side was in all cases cold and sweating and Raynaud's Phenomena occurred as previously. Continuous plethysmographic records and all other observations were made as usual.

Graph 9. (page 173) represents the record observed on injection of pilocarpine gr.1/6. By contrast, the reaction of the non-sympathectomised digit was recorded simultaneously. This has already been commented on. Cauterisation was the method of operation performed in this case.

The skin temperature of the sympathectomised digit did not vary at all at rest, being 30 - 31°C. After twenty minutes pilocarpine was administered. No effect at all was observed on the skin temperature which remained at 30 - 31°C. throughout. In contradistinction the non-sympathectomised digit became gradually cooler, the temperature being over 4°C. less than at the outset.

The pulse volume at rest maintained an ~~even~~ 0.008cc. A slight rise to 0.01cc. took place within five minutes of injection. This rise was maintained at just above 0.01cc. for over thirty-five minutes and then gradually returned to the resting level. The contrasting reaction in the non-sympathectomised digit is well seen, the steady even line of the sympathectomised digit differing in all respects from the variations and fluctuations in the normally innervated digit. Finally marked constriction is noted in the latter digit whereas the sympathectomised one remains dilated.

The digital volume similarly remains steady and even at rest. About ten minutes after injection the volume

/of the digit

of the digit slowly rises. This increase in digital volume remained until the completion of the test. A total increase in volume of 0.8cc. occurred. A slight rise in heart rate occurred.

The secretory effects of pilocarpine began about ten minutes after injection. Sweating, however, occurred about sixteen minutes after administration. The sympathectomised hand sweated in the same manner as the normally innervated extremity.

The rise in digital volume appeared to begin just before the onset of the secretory effects and sweating became clinically perceptible whilst the pulse volume was at its maximum.

In spite of profuse sweating on the sympathectomised extremity the skin temperatures and pulse and digital volumes remained at their previous or at a higher level.

The reaction of another patient in which the second, third and fourth thoracic ganglia were removed is shown in Graph 8. (page 172). This patient had been sympathectomised by open operation twelve days previously. Skin temperatures of the sympathectomised digit did not vary from the resting 30 - 31°C. throughout the period of observation following pilocarpine.

The resting pulse volume showed little variation at or about 0.008cc. Within a minute or two of injection of pilocarpine, however, the pulse volume increased. The increase reached a maximum within eight minutes and remained so for a further ten minutes. A gradual fall to the resting 0.008cc. then occurred. The maximum pulse volume of 0.015cc. was reached.

The digital volume at rest was constant, but five minutes after injection a gradual increase began which reached a maximum of 0.4cc. thirty minutes after injection.

The normally innervated extremity was a marked

/contrast.

contrast. Dilatation, as represented by an increase in pulse volume, seemed to occur in this extremity. This increase in volume was maintained for the same duration as the increase observed in the sympathectomised digit. However, a marked fall in both pulse and digital volume was the ultimate outcome.

A rather more marked rise in pulse rate occurred in this patient.

The secretory effects of pilocarpine became manifest within four minutes of injection. Sweating was well established in both sympathectomised and non-sympathectomised extremities six minutes after administration. The whole of the sympathectomised extremity except the axilla sweated.

The sympathectomised extremity did not show vasoconstriction as did the normally innervated upper limb.

In another patient the second, third and fourth thoracic ganglia were removed by transpleural dissection. On the seventh post-operative day pilocarpine gr.1/6 was given intramuscularly. No rise in skin temperature was apparent above the resting 32 - 33°C. (Graph 11. - page 188).

The pulse volume at rest averaged 0.018cc. Within a minute of injection a sharp rise to 0.30cc. was apparent. The rise was maintained at this level for about ten minutes; a tendency to fall followed, but unfortunately atropine had to be administered at this point. An immediate fall from 0.025cc. to 0.015cc. was apparent within two minutes of intravenous administration of atropine. The pulse volume soon returned to the resting level of 0.018cc. without really being in a phase of vasoconstriction.

A sharp rise in digital volume occurred on the administration of pilocarpine. In the short time before atropine was administered the digital volume had increased 1cc.

An increase in pulse rate from 80 to 100 beats per

/minute

minute occurred with pilocarpine and an even more marked rise to 140 beats per minute with atropine.

The secretory effects occurred with the same rapidity as did the increase in digital and pulse volumes. Sweating occurred on both sympathectomised and non-sympathectomised areas.

The striking feature of these three patients is the response of the pulse volume to pilocarpine. Whereas, in the normally innervated extremity, it had not been proved whether vasodilatation occurred before onset of sweating or not, the removal of inhibitory factors by sympathectomy has shown the vasodilator effect of pilocarpine. (Graph 5. - page 163, Graph 3. - page 161, Graph 6. - page 164).

In assessing the reaction of pilocarpine on the normal students it was never certain whether the slight rise in pulse volume after the injection resulted from pilocarpine only, or whether other factors, such as emotion and excitement, which naturally occur in the normally innervated extremity, had merely been inhibited. That this dilatation followed immediately after vasoconstriction, as produced by the injection, caused one to question whether dilatation resulted from the release of such factors the moment the injection had been given.

By sympathectomy the reflex arc is broken. The vessels of the extremity are thus no longer under the control of such factors as emotion, excitement, etcetera. The response, therefore, of the vessels is a direct one to the drug only. The response is not influenced any longer by central connections and the inhibitory vasoconstrictor fibres have been extirpated. Following on, therefore, pilocarpine produces the secretory effects by causing an active dilatation of the vessels concerned. As a result of dilatation the

glands secrete,and sweating and the other secretory phenomena occur.

Vasoconstriction as produced by pilocarpine occurs not as an immediate effect, but is rather a secondary phenomenon. Vasoconstriction only results in a normally innervated limb and is consequent upon the cooling induced by the evaporation of sweat. A sympathectomised extremity will not show evidence of vasoconstriction on the administration of pilocarpine. This may be due to two factors:- (1) sweating may not occur and, (2) although sweating may still occur, the cooling as induced by sweating will not cause any reaction on the denervated blood vessels.

A further period elapsed before pilocarpine was administered again. Meanwhile the opposite extremity had been sympathectomised. Therefore, the previous results obtained could be confirmed and also the reaction of the same extremity could be studied after a further lapse of time.

The patient recorded in Graph 11. (page 188) was studied one-and-a-half months later. On this occasion the pulse volume at rest was 0.008cc. The same dilatation occurred within three minutes of injection, as previously, the volume reaching 0.013cc. (Graph 12. - page 189).

The opposite extremity was sympathectomised seven days previously. The reaction to pilocarpine appears identical, dilatation occurring at the same time as on the other extremity. Both sides react therefore, in a parallel manner.

The same changes take place here in both pulse and digital volumes as on the first examination. The skin temperature is unaltered on either side.

Just over a month had elapsed after sympathectomy when pilocarpine was again administered to the patient depicted in Graph 9. (page 173). Meanwhile the opposite

/extremity

extremity had been sympathectomised nineteen days before. Both extremities were warm; sweating did not occur ordinarily; sympathectomy appeared complete. The resting pulse volume was high and appeared reasonably constant. Shortly after injection the rise in pulse volume became apparent. The rise was greater on this occasion than on the first. (Graph 13. - page 190). The rise in both pulse and digital volumes runs a parallel course in each extremity.

It is of note that, whereas sweating was clinically perceptible on the sympathectomised extremity in response to pilocarpine on the eighth post-operative day, sweating did not appear one month later! Sweating was just discernible in the recently sympathectomised extremity.

Graph 14. (page 191) shows the graphic record on administration of pilocarpine two and four months after sympathectomy of each side. In both extremities the second, third and fourth thoracic ganglia were removed.

The pulse volume of the right upper extremity maintained an even course prior to injection - 0.006cc. being the mean volume. Following injection a rise to 0.008cc. became manifest immediately. The volume was maintained at this level for the remainder of the test. A tendency to return to the resting level is apparent.

No change occurred in the skin temperatures of the right second digit and the extremity remained warm throughout. Sweating took place on this extremity, as it did all over the body, i.e. sweating occurred on both sympathectomised and on normally innervated areas.

The left upper extremity had been sympathectomised only two months prior to the test. As judged from skin temperature recording vasoconstriction occurred. A slow steady decrease in temperature occurred in the left second digit, from a resting 30 - 31°C. to 26°C. at the conclusion of the test. The left hand felt cold in marked contradistinction

/to the right

to the right.

One month later the test was repeated. The result is shown in Graph 15. (page 192). The same features are present as on the previous occasion. The pulse volume of the right third digit does not show such definite dilatation, but nevertheless the volume is slightly higher than the resting level. No evidence of constriction is present. The digital volume shows a steady increase after pilocarpine, not materially affected by the injection of atropine.

The skin temperature of the left second digit is between 27°C. and 28°C. at rest. A drop to 25°C. occurred after pilocarpine administration and fell still more to 24.5°C. after atropine had been given.

It is thus apparent that pilocarpine has caused vasoconstriction in the left upper extremity but none in the right, after both extremities had been sympathectomised by removal of the second, third and fourth thoracic ganglia on each side.

Eight months after sympathectomy of the right upper extremity and six months after the left, pilocarpine was again administered. Sweating occurred on the sympathectomised areas as previously observed.

The skin temperatures of both extremities reacted in the same way as noted two months beforehand. The temperature of the right second digit remained at or about 30°C. throughout. A sharp drop occurred in the same digit on the left side - from 29.5°C. to 27°C. Unlike the right digit, a further fall occurred to 24.5°C. after atropine had been given. (Graph 16. - page 193).

On this occasion, however, it was noticed that, although the right hand felt warm throughout, confirmed by temperature readings of the second digit, the fourth and fifth digits were cold one hour after pilocarpine administration. Whilst the temperature of the second digit was 29.8°C., those of the fourth and fifth digits were 24.5°C. and 24.1°C. respectively. It is

/likely

likely, therefore, that, as judged by skin temperatures only, the vessels of the medial two digits were constricted whilst the vessels of the second digit remained unaffected by pilocarpine.

The pulse volume of the right third digit shows, for the first time, a decrease from the resting level of 0.006cc. to 0.003cc. after pilocarpine. A tendency to vasoconstriction, therefore, first appeared eight months after sympathectomy.

In this patient vasoconstriction following pilocarpine was obtained in the left extremity as early as two months after sympathectomy. In the right extremity the first indication of vasoconstriction appeared eight months after operation and on this side vasoconstriction occurred on the medial three fingers only. Apparently the lateral two digits remained completely sympathectomised.

One other patient was observed within a year of sympathectomy. In this case sympathectomy of the upper extremity had been undertaken by removal of the second thoracic ganglion only on the right side. The left upper extremity was sympathectomised by removal of the second, third and fourth thoracic ganglia.

Sweating following pilocarpine occurred on both upper extremities and all over the body except for both lower extremities. (Graph 17. - page 194).

The pulse volume of the right digit was observed continuously. Just before pilocarpine administration the resting volume was 0.006cc. A rise to 0.008cc. occurred within three minutes of injection; this was followed by a gradual fall to 0.003cc. thirty minutes later.

The skin temperatures of both second digits fell from 31°C. and 32°C. to 28°C. after injection.

Atropine, although causing cessation of the secretory effects of pilocarpine, did not effect either skin temperatures or the pulse volume.

/Therefore

Therefore seven months after sympathectomy of both upper extremities vasoconstriction occurred following intramuscular injection of pilocarpine, as judged by skin temperature readings. This was confirmed on one side by plethysmography.

(2) Late Results:-

The majority of patients fell into this group. Late results include all patients sympathectomised one year or more previously. The most recent sympathectomy had been performed thirteen months before examination and the earliest sympathectomy had been carried out thirty years before.

Eight patients were sympathectomised for Raynaud's Phenomena, one for Buerger's Disease and one for Causalgia.

The second thoracic ganglion only was removed or cauterised in six patients, in four cases bilaterally and in one patient on one side only. In one subject the second and third thoracic ganglia were removed. One patient had Telford's operation performed nine years prviously on both sides. The stellate ganglion was removed on one side in the case of Buerger's Disease and in the causalgic patient the stellate and second thoracic ganglia had been removed.

Graph 18. (page 195) depicts the effect of pilocarpine administration thirteen months after cauterisation of the second thoracic ganglion in a case of Raynaud's Phenomena with calcinosis.

Sweating occurred on both sides of the body and appeared on the sympathectomised upper extremity, although apparently in diminished amounts.

Skin temperature readings of the second digits were reasonably steady at 31°C. at rest. An immediate fall in skin temperature in the normally innervated digit occurred after injection of pilocarpine. The sympathectomised digit also felt colder than before injection. The fall in temperature was delayed, however, and was not so marked.

/The fall in

The fall in skin temperature was maintained after atropine was given and reached the lowest readings 10 to 11 minutes later. This corresponds with the delayed cessation of sweating following atropine administration.

A slow, slight tendency to increase is apparent in the pulse volume at rest. The rise in volume continues after pilocarpine, but falls considerably in the period following atropine administration. It is probable that, here too, the decrease in digital volume results from pilocarpine and not from atropine.

It is, therefore, apparent that vasoconstriction occurred in this digit thirteen months after sympathectomy of the left upper extremity by cauterisation of the second thoracic ganglion.

Graphs 19. (page 196), 20. (page 197) and 21. (page 198) show very well the marked fall in skin temperatures and pulse volume three years after sympathectomy. Sympathectomy was bilateral by endoscopic cauterisation of the second thoracic ganglion in two cases. The remaining patient had had transpleural resection of the second ganglion on the one side with cauterisation on the other.

In each of these patients the reactions were identical. A marked fall occurred in skin temperature within a few minutes of pilocarpine administration. The digits were cold to the feel and sweating was apparent both in the sympathectomised and normally innervated areas.

The pulse volume in each case diminished considerably. 0.002cc. was the lowest value recorded in two cases, in the remaining case the pulse volume was barely registrable.

A tendency towards dilatation is apparent in Graph 20. (page 197), but this is purely transitory and is soon

/succeeded by

succeeded by vasoconstriction.

Therefore after pilocarpine intramuscularly, vasoconstriction occurred in three subjects sympathectomised three years previously.

Graph 22. (page 199) depicts a patient operated on bilaterally nine years previously for Raynaud's Phenomena. On each side Telford's operation was performed, but whereas no Horner's Syndrome is apparent on the right, the left upper eyelid droops and the left pupil has been smaller ever since. At rest both hands were cold and blue; skin temperature readings were 23 - 24°C. and the pulse volume was 0.002cc. on each side.

Spontaneous release of the spasm occurred about forty minutes later. Skin temperatures were about 34°C. - full dilatation level. The pulse volumes at this stage, however, were only 0.006 - 0.008cc. Complete release, however, was obtained in both sides 10 to 20 minutes later, the pulse volumes being 0.04cc. and 0.03cc. on the left and right sides respectively.

Pilocarpine was given at this stage. Sweating and the other secretory effects became apparent almost immediately. The pulse volume on the right rose to 0.04cc. and then dropped rapidly to 0.02cc. A similar decrease to 0.02cc. occurred on the left side but no dilatation occurred in this digit.

Atropine was given thirty minutes after pilocarpine. A sharp decrease in pulse volume, down to 0.008cc., occurred immediately. At this point, however, the secretory effects of pilocarpine are still present. It is likely, therefore, that the final vasoconstriction is not due to atropine. The changes observed in the pulse volume have not become manifest in the skin temperatures, although a tendency to

/decrease is

decrease is present.

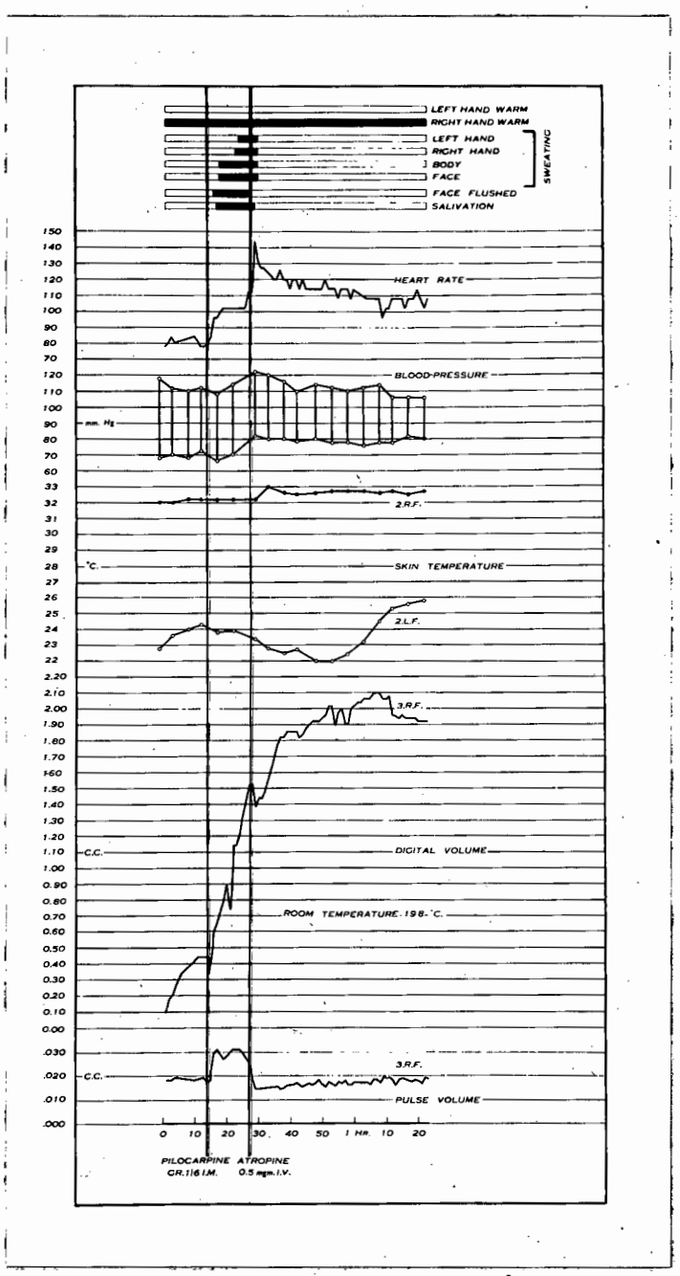
Sweating occurred all over the body except for the forehead and face. On these surfaces it was absent bilaterally throughout the test.

Graph 10. (page 174) depicts the effect of pilocarpine on a patient sympathectomised by removal of the stellate and second thoracic ganglia thirty years earlier.

The skin temperature of the sympathectomised second digit rose gradually from 25°C. to 28°C. before injection. The rise was continued rapidly to 30°C. Thereafter it was maintained for a further forty-five minutes, i.e. the duration of the test.

The pulse volume remained at 0.004cc. during the whole period of observation at rest. Only after the administration of pilocarpine did any change occur. A slow gradual increase in volume to 0.01cc. occurred over a period of fifty minutes. No sign of vasoconstriction is evident - (compare the tendency of the normally innervated extremity to vasoconstriction).

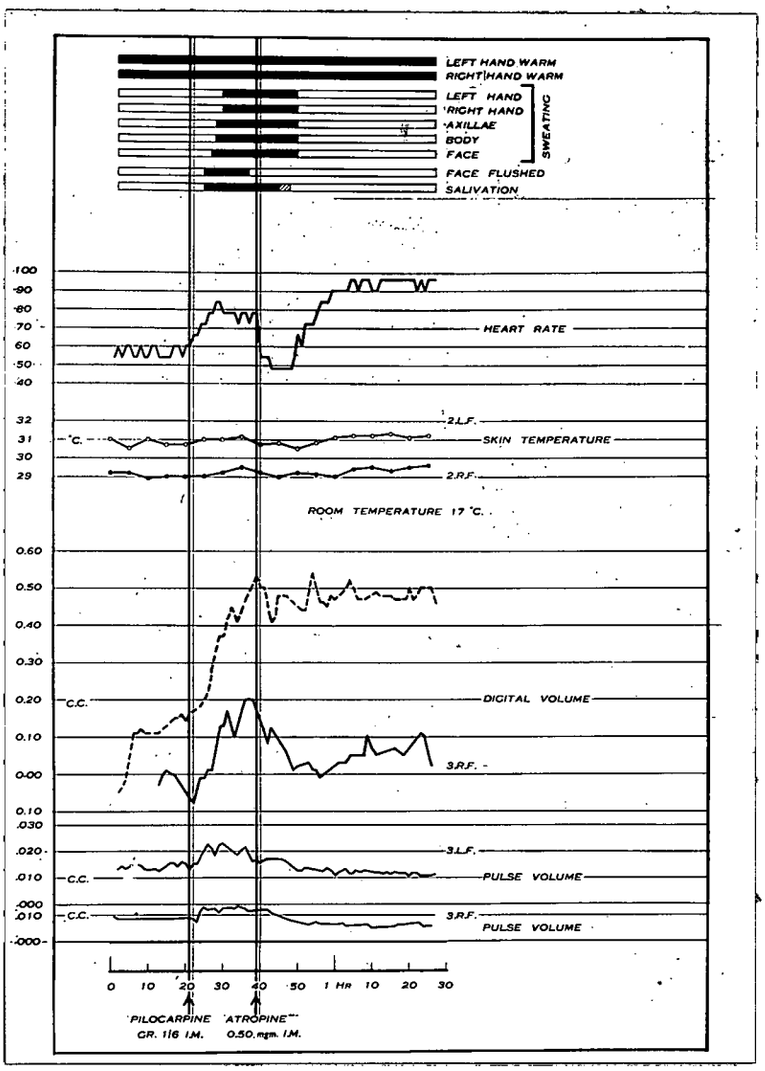
Sweating was absent on the left side of the face and forehead. It did not occur in the left axilla but was present on the left hand and forearm. The failure of the left upper extremity to show evidence of vasoconstriction is not, therefore, due to the absence of sweating which normally occurs after sympathectomy. It is, therefore, apparent that sympathectomy is still complete thirty years after operation.



GRAPH 11.

Same case as in Graph 7.

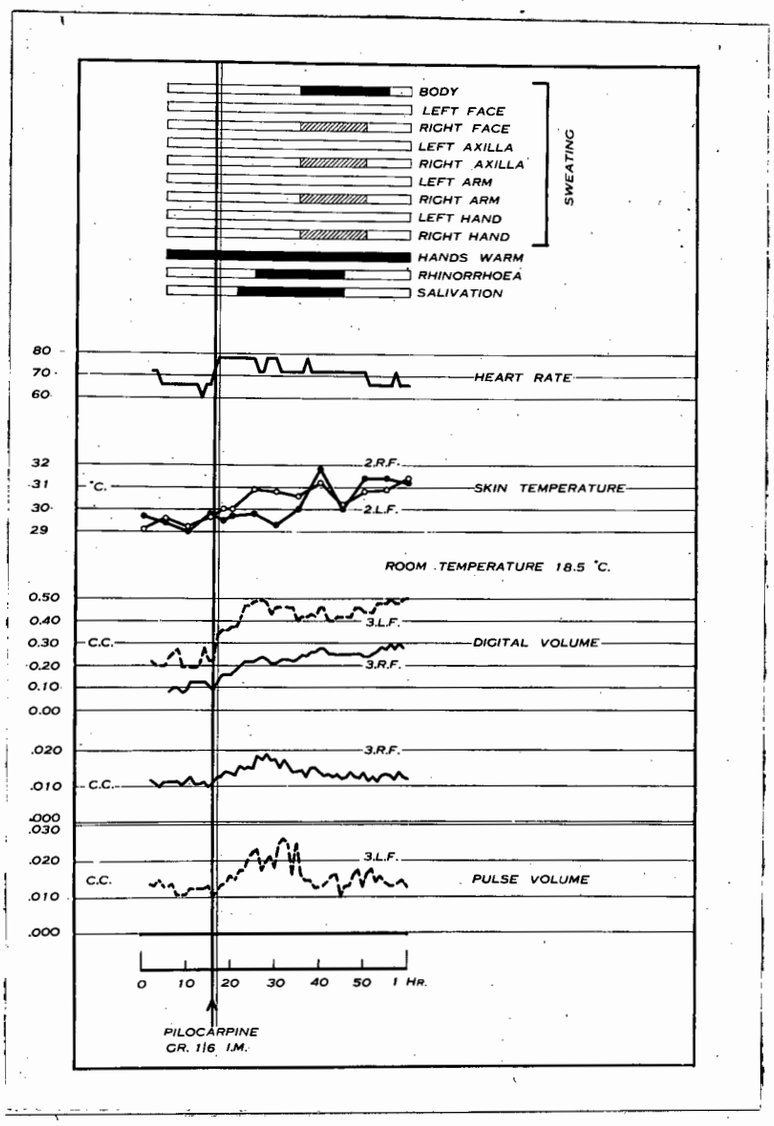
The effect of pilocarpine six days after removal of Right Th.2, Th.3 and Th.4.



GRAPH 12.

Same case as in Graph 7.

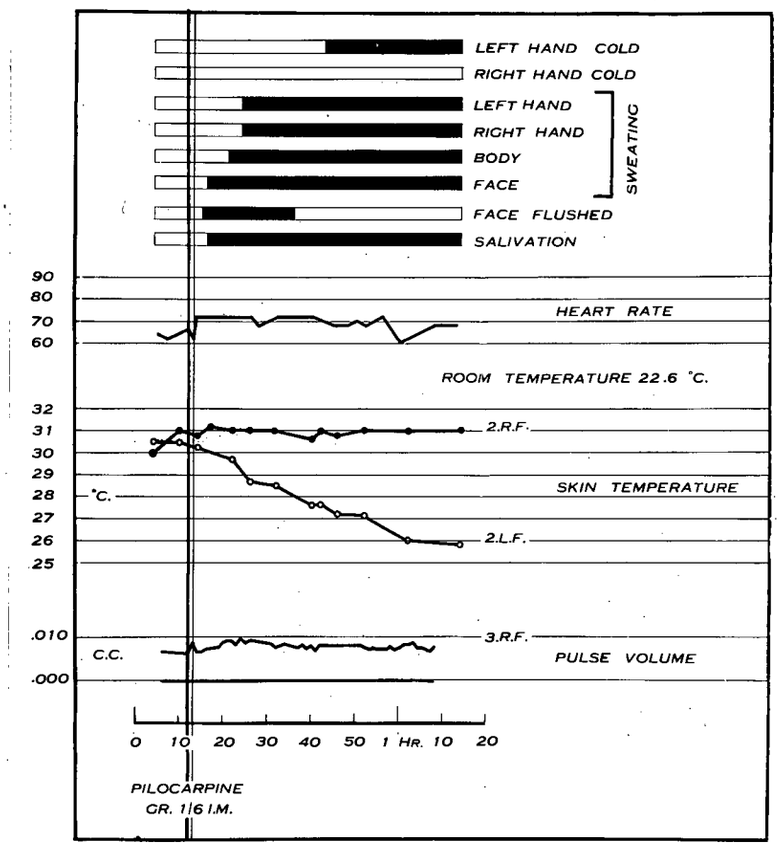
Six days after removal of left Th.2, Th.3 and Th.4 and one-and-a-half months after removal of right Th.2, Th.3 and Th.4.



GRAPH 13.

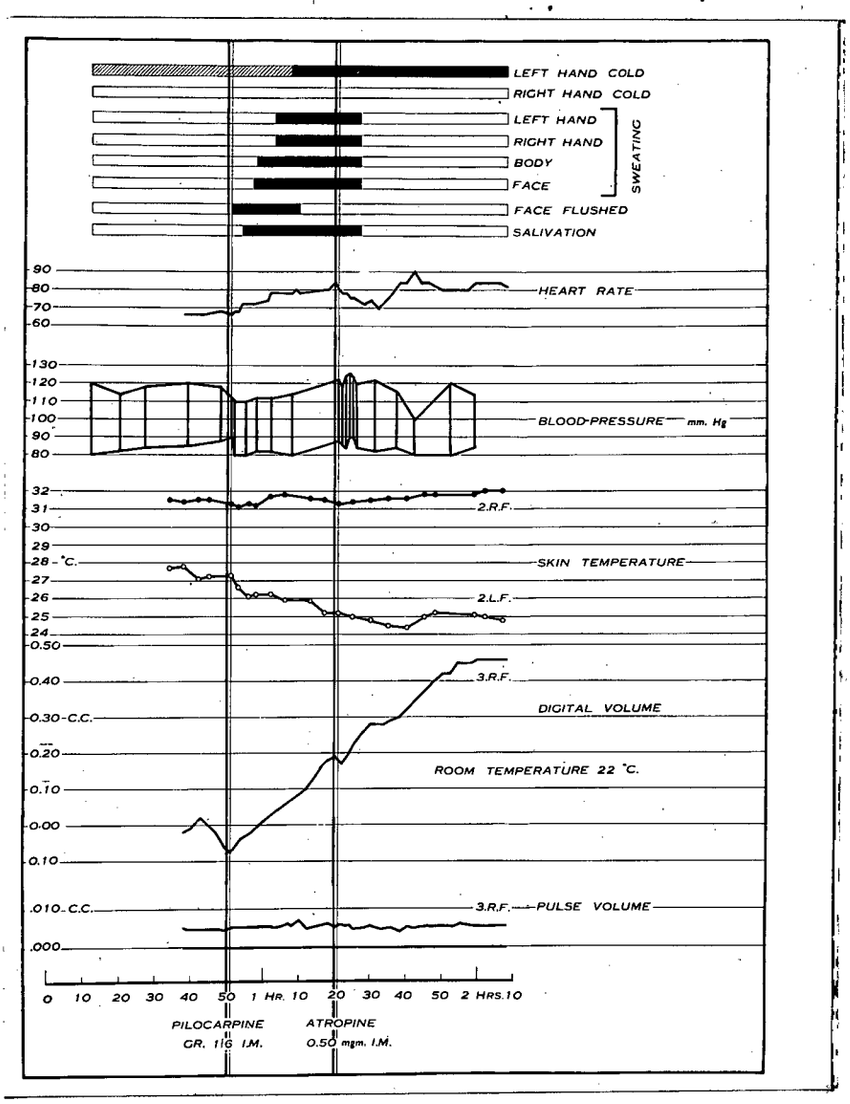
Same case as in Graph 9.

Nineteen days after removal of Right Th.2, Th.3 and Th.4 and one month after cauterisation of Left Th.2, Th.3 and Th.4.



GRAPH 14.

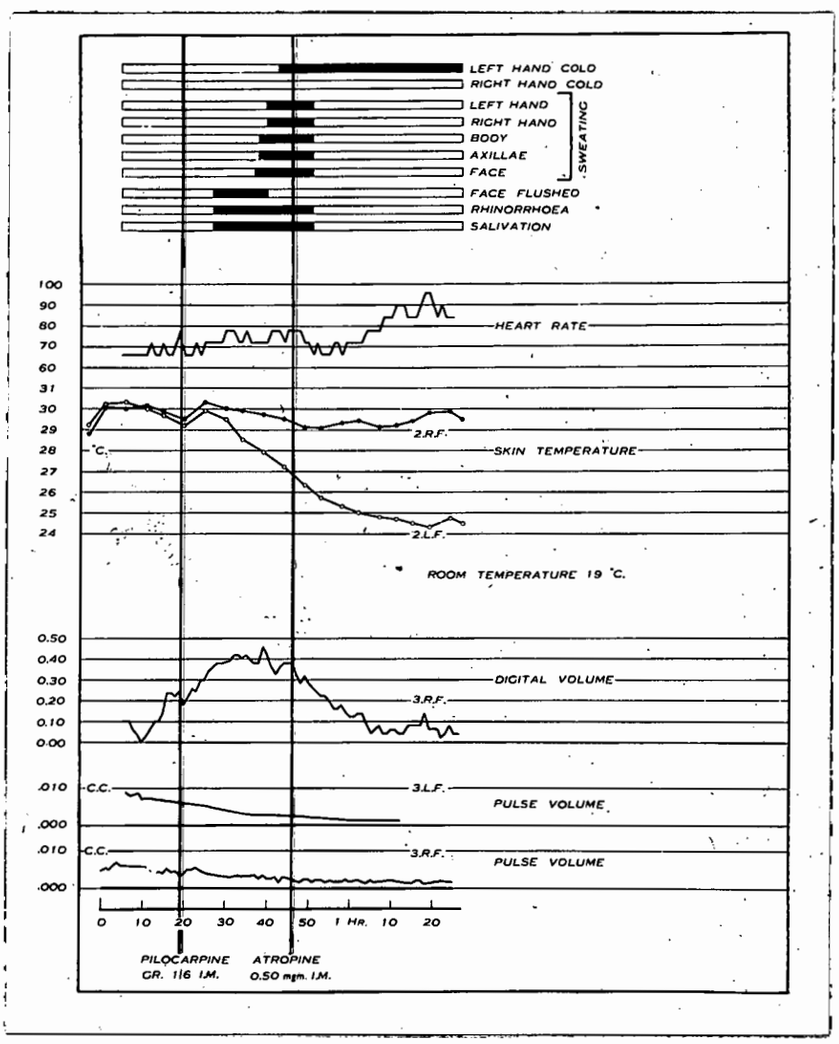
The effect of Pilocarpine.
Two months after cauterisation of Left Th.2, Th.3 and Th.4.
and four-and-a-half months after removal of Right Th.2, Th.3, Th.4.



GRAPH 15.

Same case as in Graph 14.

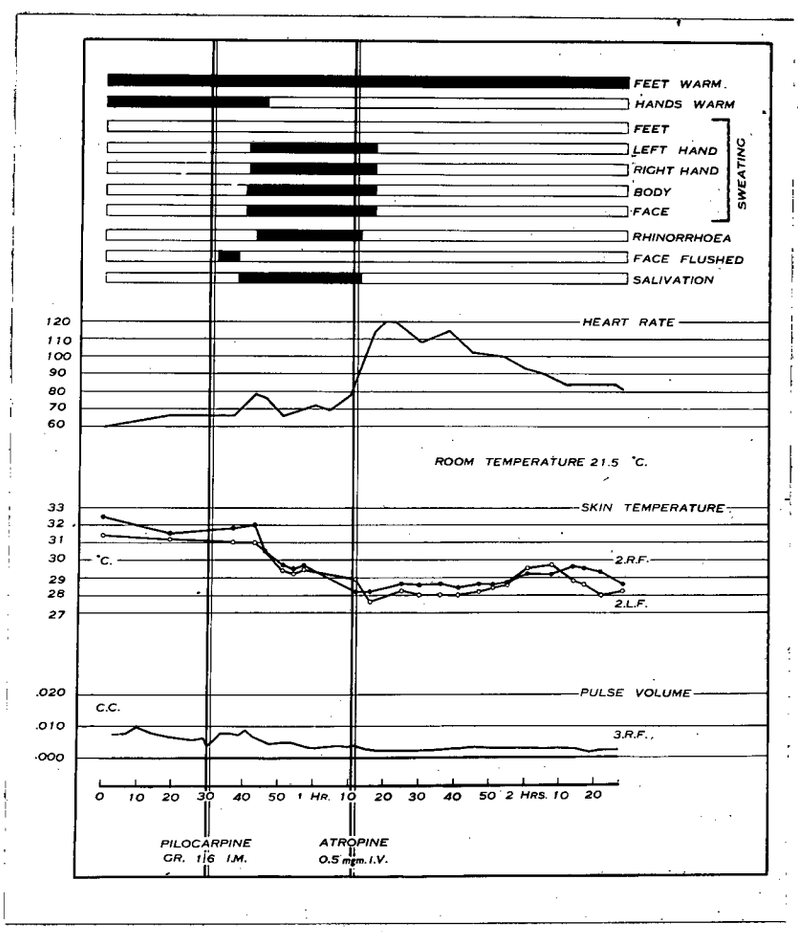
One-and-a-half months later.



GRAPH 16.

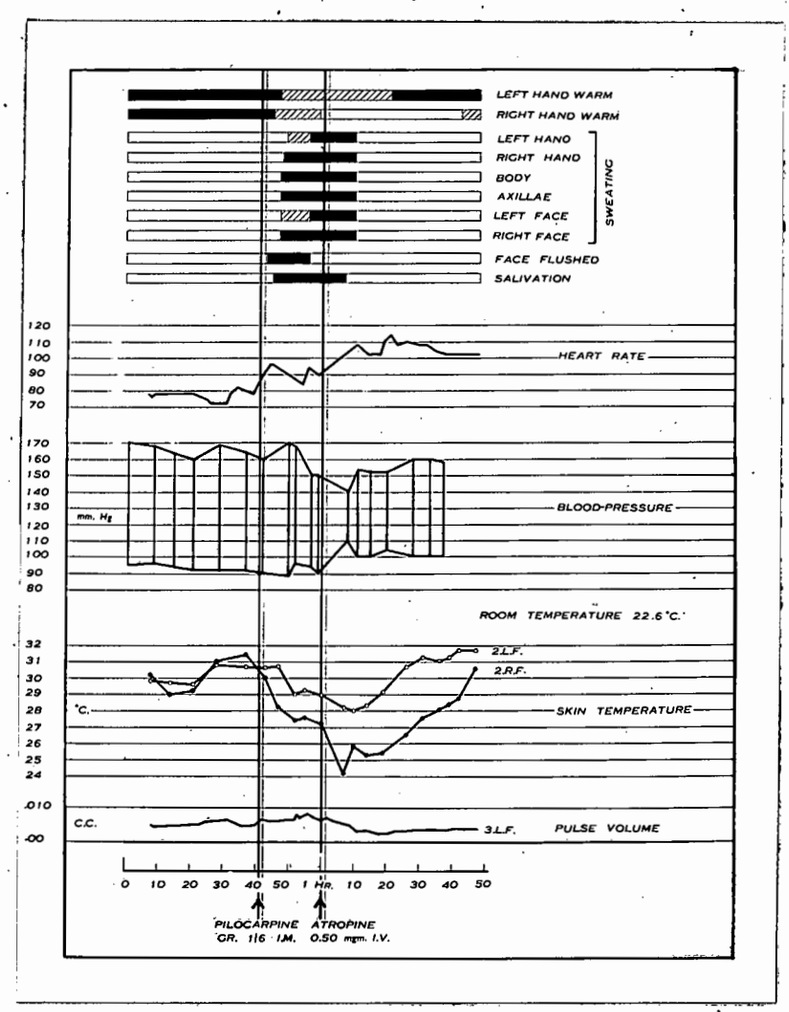
Same case as in Graph 14.

Three-and-a-half months later.



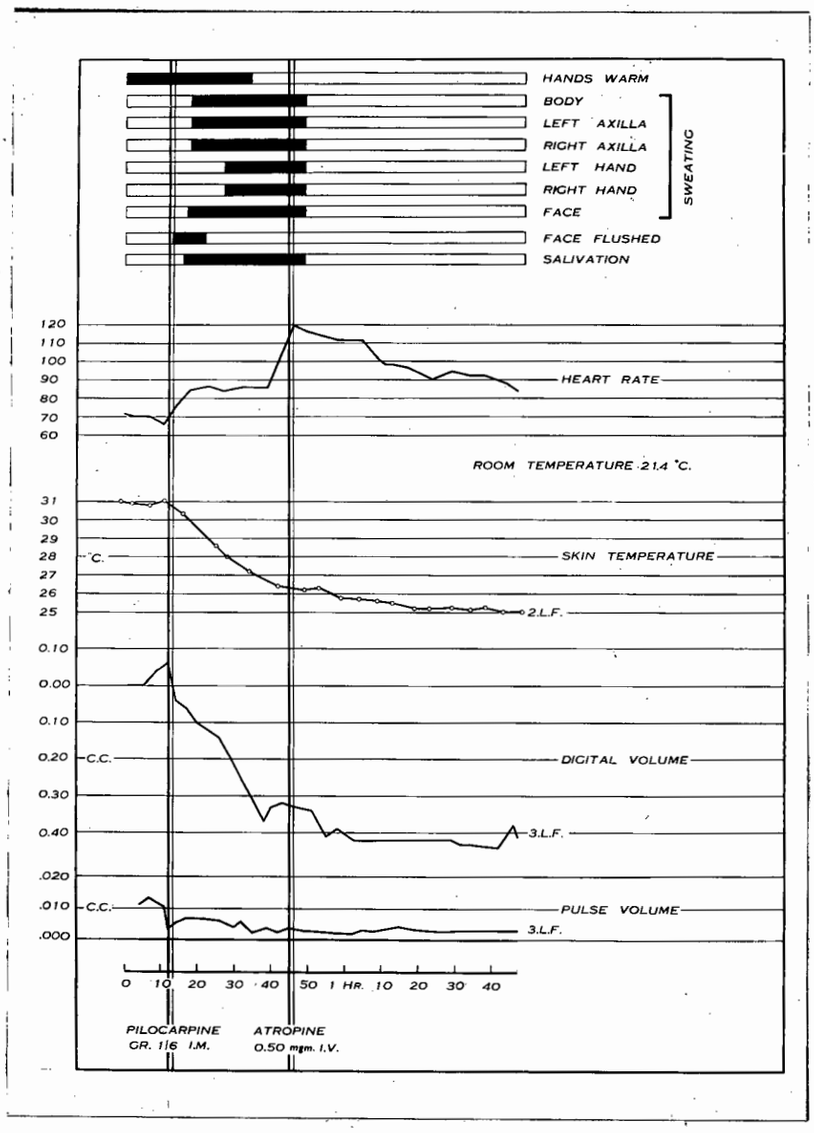
GRAPH 17.

The effect of Pilocarpine
Five months after removal of Right Th.2.
and six months after removal of Left Th.2, Th.3 and Th.4.



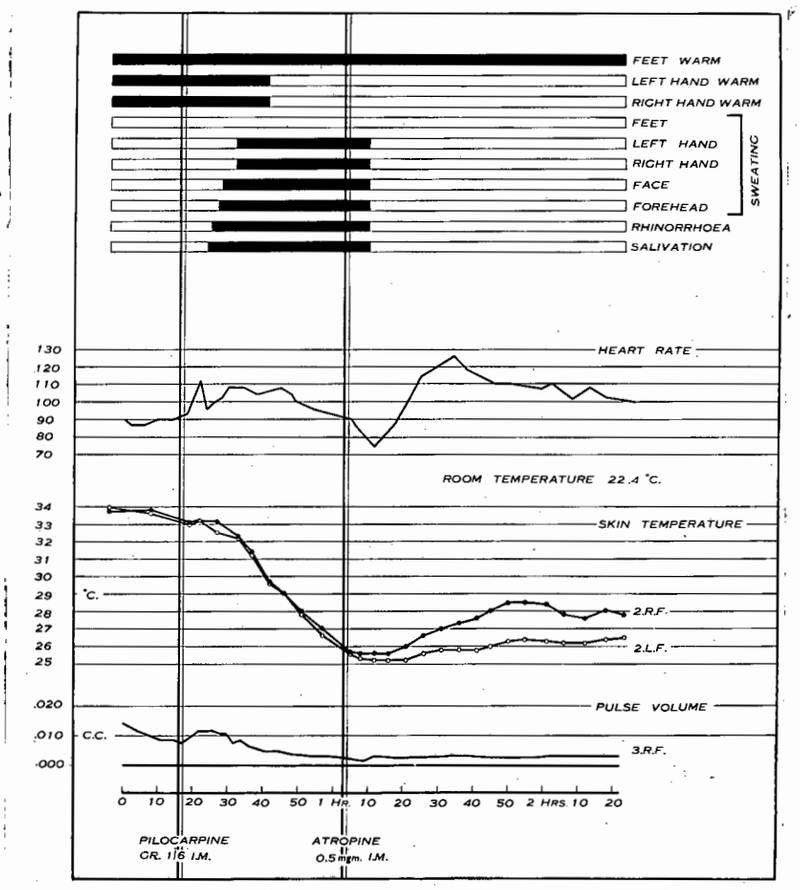
GRAPH 18.

The effect of Pilocarpine
Fourteen months after cauterisation of
Left Th.2.



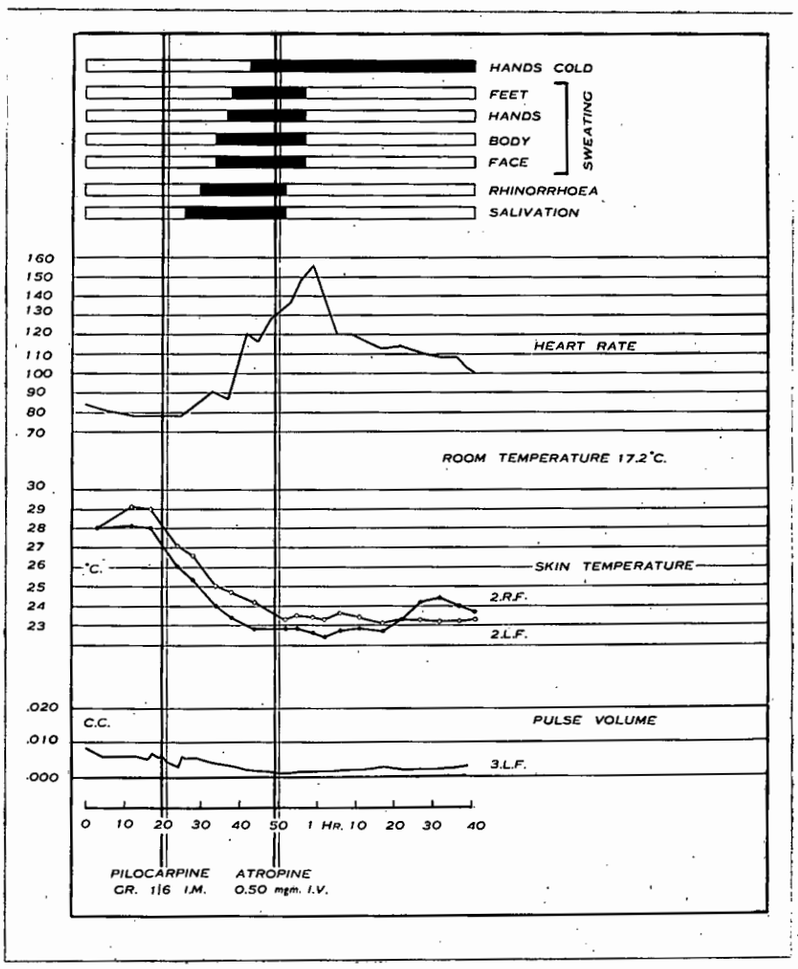
GRAPH 19.

The effect of Pilocarpine three years after bilateral cauterisation of Th. 2.



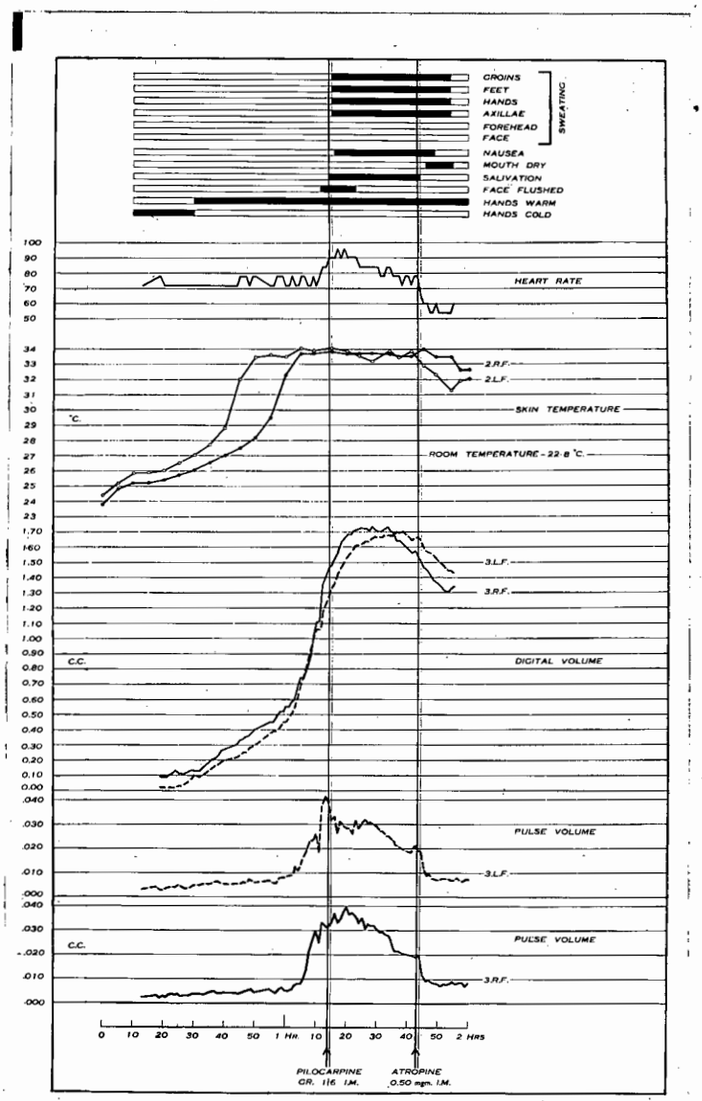
GRAPH 20.

The effect of Pilocarpine,
Three years after
bilateral cauterisation of Th.2.



GRAPH 21.

The effect of Pilocarpine nearly three years after cauterisation of Right Th.2 and removal of Left Th.2.



GRAPH 22.

The effect of Pilocarpine
over nine years
after bilateral Telford's operation.

Summary and Conclusions:

Sympathectomy was performed for Raynaud's Phenomena in fifteen of the patients examined. In one patient Raynaud's Phenomena was associated with calcinosis, and cervical ribs were removed in one subject. Causalgia was the reason for sympathectomy in one patient and thrombo-angiitis obliterans in another.

As noted above, the interval between sympathectomy and re-examination varied from the immediate post-operative days to thirty years after sympathectomy. The time interval varied particularly in those patients with Raynaud's Phenomena, which group constitutes over 80 percent. of the patients examined.

Five patients with Raynaud's Phenomena were re-examined with pilocarpine within the first year after sympathectomy. Three of these patients were examined within the first post-operative days. In these patients pilocarpine did not produce any vasoconstriction and no Raynaud's Phenomena occurred subsequent to injection of the drug.

One patient showed Raynaud's Phenomena after pilocarpine six months after sympathectomy. In the remaining patients pilocarpine produced a fall of skin temperature in one extremity four months after sympathectomy. Three months later, i.e. nearly seven months after sympathectomy, the other extremity showed diminution of the pulse volume after pilocarpine, although the skin temperature remained relatively steady. (Graph 16. - page 193). On this occasion a fall in skin temperature, however, was present in the medial three fingers.

Thus vasoconstriction has resulted from pilocarpine within six months of removal of the sympathetic nerve supply

/to the upper

to the upper extremity in two out of five patients. The remaining three patients had been observed for a shorter interval and it is not possible to state that Raynaud's Phenomena would not recur in these cases.

The remaining ten patients suffering from Raynaud's Phenomena were all observed at least one year after sympathectomy. All these patients responded to pilocarpine by eventual vasoconstriction. In some cases actual Raynaud's Phenomena were reproduced.

It is apparent that, except for the three patients observed at too short an interval after sympathectomy, vasoconstriction has resulted in this group of patients after sympathectomy had been performed. This feature is a common one no matter what type of operation was undertaken.

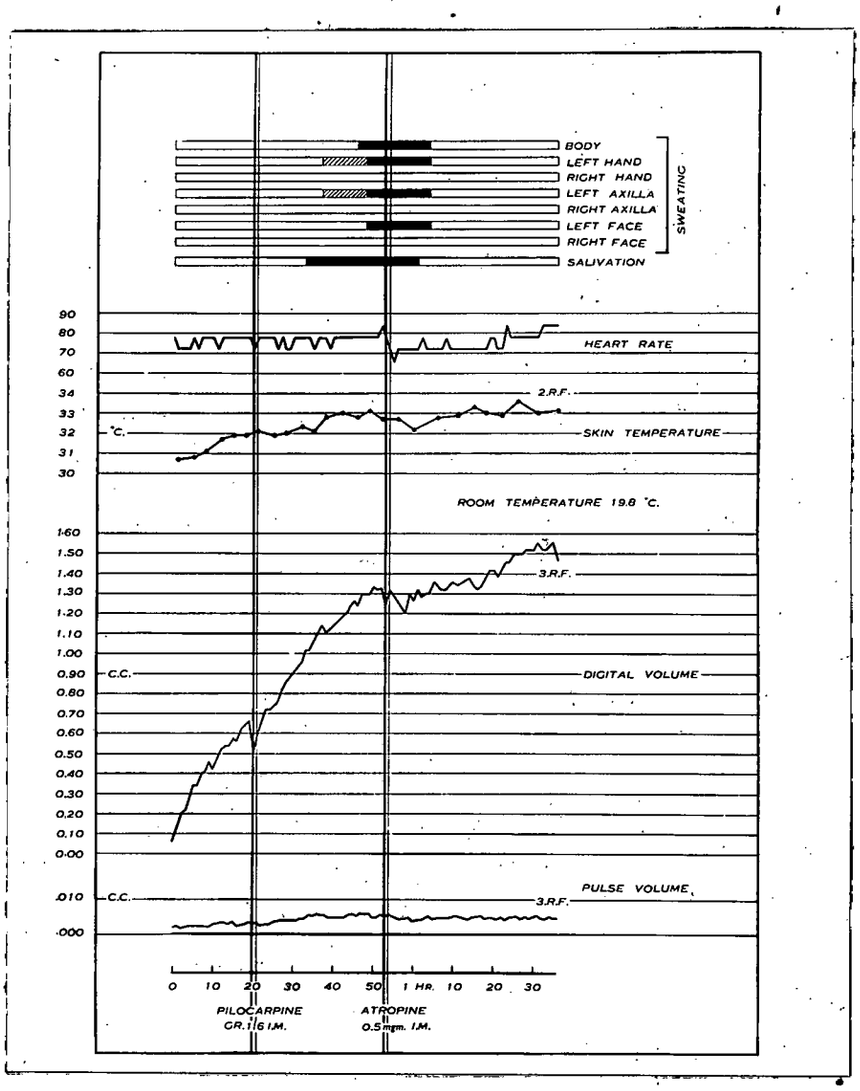
Whether only the second thoracic ganglion was removed or whether the operation was extended downwards to include the third thoracic ganglion or the third and fourth, all constricted after pilocarpine. In one subject Telford's operation had been undertaken. In this patient, too, vasoconstriction resulted.

The method of operation obviously played no part in determining whether vasoconstriction would ensue or not. Actual dissection by transpleural thoracotomy, or cauterisation of the ganglia and trunk by the thoracoscope, or sympathectomy via a posterior approach did not affect the outcome in any particular case.

One patient with Buerger's Disease was given pilocarpine nine years after removal of the stellate ganglion. No vasoconstriction resulted in this extremity. (Graph 23. - page 203). In this patient the sympathectomised area did not sweat, although sweating occurred in the normally innervated areas.

/The remaining

The remaining subject, a case of causalgia, had been sympathectomised thirty years previously by removal of the stellate and second thoracic ganglion. No evidence of vasoconstriction resulted after pilocarpine. The extremity is thus apparently still completely sympathectomised.



GRAPH 23.

The effect of Pilocarpine nine years after Right Stellatectomy.

4. Plethysmography.

The value of the optical digital plethysmograph in assessing the circulation of the extremities has been repeatedly emphasised by Goetz (1943, 1945, 1946). From the original model (Goetz - 1935, 1939) the plethysmograph has been developed considerably. Although originally it was possible to record the blood flow through only one digit at a time, the apparatus has been developed so that two digits can be examined simultaneously (Goetz - 1948). This has been of inestimable value because of the possibility of observing the reaction of both a normally innervated and a sympathectomised extremity to the same stimulus simultaneously.

The methods generally used for measuring the tone of the peripheral blood vessels furnish only indirect indices of the blood flow. Thus, skin temperature measurements or colorimetric readings, which have been used to a large extent in many clinics to show changes in the peripheral circulation, do not by themselves offer the information obtained from the plethysmograph. The plethysmograph in association with skin temperature measurements furnishes an accurate concept of the capacity of the vascular bed.

The methods adopted by Goetz have been used throughout the plethysmpgraphic examination of all the patients examined in this series and have followed the same routine in each patient.

Method.

All patients were clothed in pyjamas and reclined on the couch specially devised by Goetz (1948). Either one or two blankets completely covered the patients, except for the head and face and the distal part of each extremity. Heat dissipation was thus prevented.

The room temperature was estimated by an ordinary

/mercury

mercury thermometer. Although considerable variation occurred from day to day, the degree of change during the actual test amount to very little.

In order to obviate any change in the circulation attributable to environmental conditions, the patient remained on the examining couch for 30 to 60 minutes before any investigations were begun. In this way the pulse volume recorded at rest is probably a true reflection of the circulation at that temperature. Thus only after this interval, could the changes occurring at rest be standardised and plethysmographic examination start.

Initially Goetz was able to record the changes occurring in only one digit at a time (1943, 1946). However, the plethysmograph has been developed recently and the blood flow of two digits of the same or different limbs can be recorded simultaneously on one and the same film. (Goetz - 1948). The advantage of this is obvious and the vascular reactions of a normal limb can be compared with that of a sympathectomised extremity at one and the same time.

After connecting the digit(s) to be examined to the apparatus by means of the glass container(s), a sample tracing is recorded of the patient during rest. Skin temperature measurements are recorded at this stage, too, and any other investigation that is necessary.

Both lower extremities are then immersed in the water bath to a point about six inches above the ankle. The bath, designed by Goetz (1948) contains water thermostatically heated to a temperature of 43 - 45^{o}C.

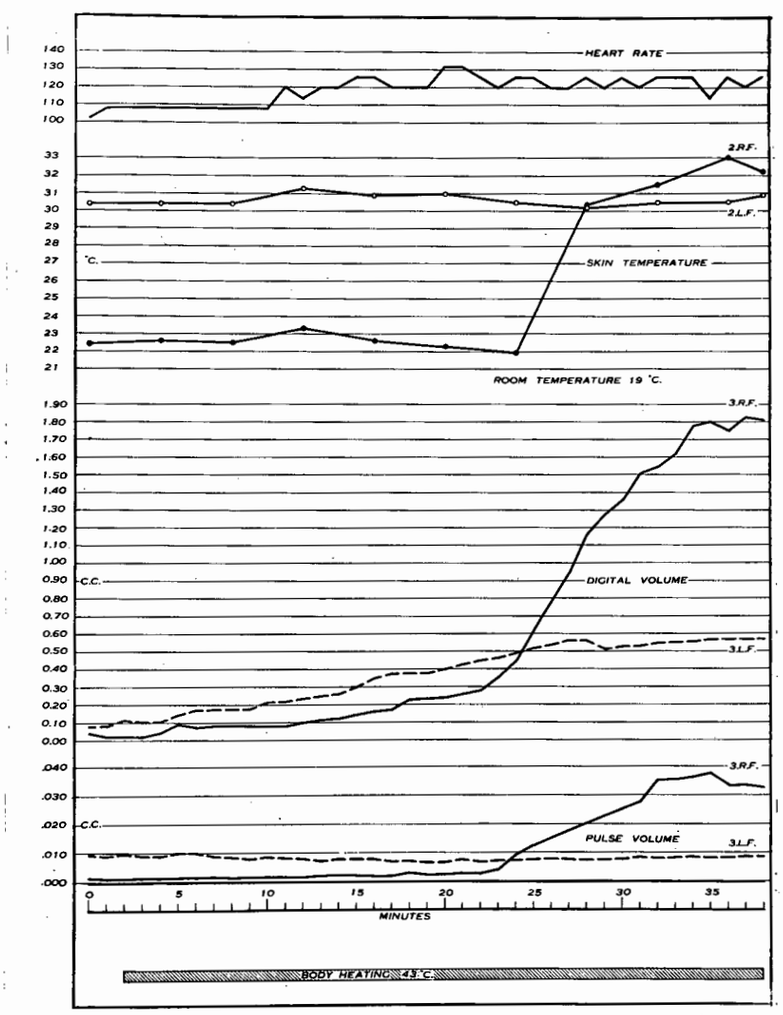
This thermo-regulatory body heating is continued for a period of 30 to 35 minutes, as suggested by Gibson and Landis (1930). A continuous plethysmographic record can be taken throughout the period of body heating. This was done in several patients and the changes in blood flow were then drawn graphically. (Graph 24. - page 207). In the majority

/of patients

of patients a continuous tracing is not necessary and a plethysmograph at the end of thirty-five minutes will yield any necessary information.

Skin temperature measurements are again recorded after body heating. Any further test, e.g. effect of a deep breath on the pulse volume, is then performed and the test concluded.

The immersion bath has proved useful, too, in determining the reflex changes occurring in a fully dilated extremity, as the result of immersion of the extremities in iced water. The bath is a handy receptacle and except for emptying it, the patient is not disturbed at all. The patient remains on the couch, connected to the apparatus by the glass container around the digit.



GRAPH 24.

Same case as in Graph 8.

The effect of thermo-regulatory body heating.

Left Th.2, Th.3 and Th.4 removed eleven days previously.

In assessing the vasomotor tone of the extremities Gibbon and Landis (1932) first noted that immersing the forearms in water at 43 - 45°C. produced vasodilatation of the lower extremities. The authors observed that this vasodilation may result in two ways:- (1) the response may be due to sensory impulses from the limbs immersed in hot water, or it may be due to (2) the heat carried into the body by the venous blood, returning from the warmed limbs.

However, they produced evidence to show that the hypothesis, that the vasodilatation results from afferent nerve impulses originating in the immersed limb, is not tenable. It was apparent that the vasodilator response depends on the return of warmed blood from the immersed extremity.

The effector mechanism of the dilator response had been studied by Lewis and Pickering (1931). They showed that the response is absent in the sympathectomised extremity. This method, therefore, could be used in determining whether the sympathetic innervation of vessels of the limb had been lost.

Prior to Gibbon and Landis' observation, several methods of producing vasodilatation had been suggested. Brown (1926) had produced peripheral vasodilatation by the injection of typhoid vaccine. Morton and Scott (1930) induced vasodilatation of the lower limbs by means of spinal anaesthesia and later proposed the use of general anaesthesia - ether, nitrous oxide or ethylene, to produce the same effect (1931). Injection of peripheral nerves with novocaine has also been used to produce local vasodilatation by White (1930), Lewis (1929) and Scott and Morton (1931).

Immersion of the lower extremities in a water bath at 43 - 45°C. for thirty-five minutes has been the standard

/method of

method of investigating the peripheral circulation of the upper extremities at the Groote Schuur Hospital.

In view of the fact that the effector mechanism of dilatation of the peripheral vessels is mediated through the sympathetic nerves, this thermo-regulatory body heating test has been used in all the patients examined in this series.

The effect of body heating on both a normally innervated and a sympathectomised extremity is shown in Graph 24. (page 207). The patient, a case of Raynaud's Phenomena, had been sympathectomised by the removal of the left second, third and fourth thoracic ganglia. The pulse volume at rest of the normally innervated extremity was barely registrable. The sympathectomised extremity, however, had a resting volume of 0.01cc. Twenty-five minutes after the onset of thermo-regulatory body heating, the pulse volume of the normal side had increased to 0.01cc. and dilatation was maintained, reaching nearly 0.04cc. after thirty-five minutes. The sympathectomised extremity, however, did not dilate in the same manner and the volume after thirty-five minutes was, if anything, slightly less than at rest.

Figure 54. (page 221) is a copy of the plethysmographic tracing taken at rest and after body heating in the patient depicted in Graph 24. (page 207). The upper tracing in each case is the sympathectomised digit. The relatively small change in pulse volume is obvious. The change in the normally innervated digit from a barely registrable volume to 0.04cc. after body heating is striking.

As Goetz (1943) emphasises, since reflex dilatation of the digital vessels results mainly from the inhibition of vasoconstrictor tone and, therefore, is dependent upon the integrity of the sympathetic nerve supply, no change is

/expected

expected in the rate of blood flow of sympathectomised limbs. The pulse volume remains at the initial level. Goetz in the same paper, has pointed out that there may be an actual decrease in the pulse volume. He emphasises that this decrease is not due to the environment, which remains the same; and, the extremity being sympathectomised, is not due to central impulses. It is due to a passive effect resulting from the dilatation of the vascular tree in the other normally innervated areas.

As a result of the decrease in vasomotor tone in the areas under normal sympathetic control, the unaltered vasomotor tone of the sympathectomised extremity presents itself as a relative increase in tone. The blood follows the path of least resistance and, therefore, a decrease in blood flow through the sympathectomised extremity ensues.

A similar decrease in pulse volume of the sympathectomised extremity is seen in Figure 55. (page 221). From a pulse volume of over 0.03cc. at rest, after thirty minutes thermo-regulatory body heating, the pulse volume had decreased to just over 0.02cc.

The changes in digital volume reflect those pertaining to the pulse volume. There is an increase in the volume of the normally innervated digit by nearly 2cc. The sympathectomised digit, however, has increased 0.5cc. after the same degree of body heating.

The skin temperature of the sympathectomised digit remained at 30 - 31°C. throughout the duration of the test. On the normally innervated digit the skin temperature remained at 22°C. for over twenty minutes after the onset of body heating. At this time, however, the pulse volume had risen from barely registrable resting level to 0.01cc. Only four minutes later did any appreciable increase in skin temperature take place and in this interval the pulse volume,

/had risen to

had risen to 0.02cc.

This feature of the delay in the rise of skin temperature whilst the pulse volume has risen to 0.01cc. emphasises Goetz's claim of the value of plethysmography. The skin temperature furnishes only an indirect index of blood flow, whereas the most sensitive change in blood flow has been easily recorded plethysmographically.

A rise in pulse rate from a resting 110 per minute to 125 per minute took place as a result of body heating. This change in pulse rate is observed in most patients. It is shown also in Figure 55. (page 221).

Graph 25. (page 222) shows the changes consequent upon body heating in a patient after bilateral sympathectomy of the upper extremity by removal of the second, third and fourth thoracic ganglia about one month previously. At a room temperature of 18°C. the resting pulse volumes of both sides was over 0.01cc. At the end of thirty-five minutes thermo-regulatory body heating the pulse volume was still just over 0.01cc. The pulse volume of the right middle finger was, if anything, slightly less than at the outset.

The close similarity of the changes in the pulse and digital volumes is well shown. There has been no increase in the latter. Similar changes are reflected in the skin temperature records. The heart rate has not altered in this patient, in response to body heating.

The changes in pulse volume are reflected in Figure 56. (page 223). The upper tracing is the left middle finger in each case. An actual decrease is apparent in the pulse volume of the right middle finger after body heating.

Two years after cauterisation of the left second thoracic ganglion, reflex body heating was performed on the

/patient.

patient observed in Graph 26. (page 224). The pulse volume of the left middle finger was over 0.01cc. at rest. After thirty minutes the pulse volume rose to 0.023cc. An increase in digital volume of 1.3cc. took place and the skin temperature rose from a resting 28°C. to over 33°C.

The response of all three components observed during the test, viz. pulse volume, digital volume and skin temperatures, to thermo-regulatory body heating in this patient indicates that vasomotor tone is present. Although the resting pulse volume is relatively high at the room temperature, the increase in volume indicates that some sympathetic control has been relased. Further studies with other reflex phenomena confirm this observation.

Thus, should an extremity, that has undergone sympathectomy, react to reflex body heating by inhibition of vasoconstrictor tone and the pulse volume increase to the normal vasodilatation level, it is likely that sympathectomy has either been imcomplete originally or that regeneration has taken place. Goetz (1948) describes a subject where the former was the case. Subsequent complete removal resulted in this test showing the changes expected in a completely sympathectomised extremity.

Reflex body heating on the same patient but on the sympathectomised opposite extremity shows the same release of vasoconstrictor tone. (Graph 27. - page 225). Other observations also confirm the integrity of the effector mechanism on this side.

Fourteen patients were examined by the thermo-regulatory body heating test to determine the presence or absence of vasomotor tone.

Five patients were examined within a year of sympathectomy and in these reflex body heating failed to produce

/any rise in

any rise in pulse volume from the resting level. The assumption, therefore, is that sympathectomy is complete in these cases.

Of the eight patients examined one year or more after sympathectomy, reflex body heating resulted in vasodilatation in all. Sympathetic tone has returned in these cases. In this group the second thoracic ganglion only was removed in four patients bilaterally; in one patient the second thoracic only and the second and third thoracic ganglia were removed on each side respectively. In one case both second and third thoracic ganglia were removed on each side; in another Telford's operation had been performed bilaterally and in yet another the third ganglion only on each side.

Reflex body heating in the sympathectomy of thirty years' standing is depicted in Graph 28. (page 226). A rise in pulse volume from a resting 0.005cc. to 0.01cc. after thirty minutes occurs. The normally innervated extremity was obviously fully dilated at the outset and no change occurred therein. The considerable fluctuation in the pulse volume of the normal side is striking compared with the minimal changes occurring in the sympathectomised digit.

That this failure of the pulse volume of the sympathectomised extremity to dilate after reflex body heating is not due to an organic occlusion, is easily shown. By immersing the extremity in warm water at 45°C. for ten minutes, i.e. by the application of local heat, dilatation results. This has been demonstrated by Goetz (1948) and is well shown in this last patient. Figure 2. (page 67) shows both hands after thirty minutes body heating. Direct heat, as indicated above, was then applied to the sympathectomised extremity. A further dilatation ensued to the maximum dilatation level. (Figure 1. - page 67).

/In 1933 Goetz

In 1933 Goetz demonstrated that a profound peripheral constriction resulted from a single deep breath. This diminution in blood flow is reflex in nature, since it can be abolished by sympathectomy (Goetz - 1935). The reflex apparently originates in the lungs (Peters - 1939), and is set in train only by the inspiratory phase. It is dependent upon the integrity of the sympathetic pathways.

The reaction is easily recorded when the extremity is moderately or fully dilated but under ordinary conditions vasoconstriction may be absent because of the already high vasomotor tone. Thus the reflex effect of a deep breath is always tested when the extremity is well-dilated.

The reaction in a normally innervated extremity and in a sympathectomised extremity is shown in Figure 57. (page 227). The height of the pulse volume is unaffected by the single deep breath nor is there any alteration in the digital volume of the sympathectomised side. In the normally innervated extremity a profound decrease in pulse volume occurs. At the same time the digital volume decreases rapidly. A gradual return to normal then occurs.

Figure 58. (page 227) shows the effect of a deep breath on both a normally innervated extremity and a sympathectomised extremity at the same time. The same changes as noted above occur in a striking manner. Where possible the test was recorded, as it is a simple indication of the integrity or otherwise of the sympathetic innervation to the extremity.

A yawn or a sigh has exactly the same effect as a deep breath and, on occasion, the accidental recording of such a stimulus has yielded invaluable information. The accidental recording of a sigh is shown in Figure 59. (page 228). Vasoconstriction occurs as shown by the fall in pulse and digital

/volume.

volume. This patient had been sympathectomised three years previously by cauterisation of the second thoracic ganglion. As judged by this response, the sympathetic supply to the extremity is intact. This is confirmed above by the response to reflex body heating.

Goetz (1946) has also pointed out that other sensory stimuli may result in peripheral vasoconstriction. Thus an unexpected noise, pain, single or multiple pinpricks, emotional content of thought or mental strain may result in vasoconstriction Even the anticipation of these stimuli may have the same effect. All of these are well-known vasoconstrictor reflexes and as such are not obtained after sympathectomy. Absence of vasoconstriction following any such sensory stimulus, provided moderate or full dilatation is present, indicates interruption of the sympathetic innervation of the part concerned. Conversely the presence of such vasoconstriction would mean the integrity of the sympathetic supply.

The effect of multiple pinpricks on the face, which normally result in vasoconstriction, is shown in Figure 60. (page 228). No change is observed in the pulse or digital volumes thirty years after sympathectomy. A similar absence of vasoconstriction is seen in Figure 61. (page 229), in a patient with Raynaud's Phenomena one year after sympathectomy. The absence of sympathetic innervation to the extremity has been confirmed in each case by other tests.

The most striking reflex vasoconstriction is observed when the feet, if the arms are being tested, are immersed in cold water. Normally an immediate vasoconstriction occurs. If, however, the sympathectomy is satisfactory, no change occurs in the pulse or digital volume as recorded plethysmographically. Actually, it is theoretically possible for a slight dilatation to ensue.

/Figure 62.

Figure 62. (page 229) shows the effect, observed simultaneously on both a normally innervated and a sympathectomised extremity. Whereas a fall in both pulse and digital volume is apparent within a few seconds in the normal limb, the pulse and digital volumes manifest no change at all in the sympathectomised extremity. The test was repeated again with the identical result.

In Figure 63. (page 230) the same effect is observed eighteen months after cauterisation of the second and third thoracic ganglia on one side. Both feet were immersed in cold water and a fall in pulse volume and digital volume occurred immediately, in the normal side. On the sympathectomised side, however, no decrease occurred in either pulse or digital volumes.

In all, thirty extremities, in which some form of sympathectomy had been undertaken during the previous thirty years, were examined plethysmographically. If vasomotor tone, as judged by thermo-regulatory body heating and the response to the various reflex vasoconstrictor stimuli, was present, it indicated that the vessels of the extremity were under the control of the sympathetic nervous system. If, on the other hand, vasomotor tone was absent, as judged by the same criteria, the extremity was considered not to be under any sympathetic control.

In determining the results obtained by plethysmography three factors have to be considered:- (1) the nature of the disease, (2) the type of sympathectomy, and (3) duration of time after sympathectomy.

Table I. shows the results as determined in the type of lesion for which sympathectomy was done. Twenty-seven (or 90 percent.) of all sympathectomies were performed for Raynaud's Phenomena. One of these was associated with a cervical rib, and one other had associated calcinosis. No

/other etiological

other etiological factor was found in the remaining subjects. Vasomotor tone was present in seventeen (63 percent.) and absent in the remaining ten (37 percent.) At first sight sympathetic function had returned in 63 percent. of all cases sympathectomised for Raynaud's Phenomena.

Although only three cases of non-vasospastic conditions are included in the series, not one case shows a return of sympathetic function after operation. Causalgia was the reason for operation in two cases, and thrombo-angiitis obliterans in the remaining case. As will be seen later, the type of operation differed in the two groups.

In the group of ten extremities operated on for Raynaud's Phenomena, where vasomotor tone was absent, only three had been observed for more than one year after operation. These three extremities had been sympathectomised just over one year before re-examination and although they have not been examined again, one case, representing two extremities, has since noticed return of Raynaud's Phenomena. Thus, only one extremity out of twenty (5 percent.) has a complete lasting absence of vasomotor tone. The seven extremities included in this group have not been followed for a sufficient time to be finally assessed.

TABLE I.

Disease.	Number.	VASOMOTOR TONE.	
		Present.	Absent.
Raynaud's Phenomena	27	17	10
Thrombo-angiitis Obliterans	1	0	1
Causalgia	2	0	2

/The nature

The nature of the sympathectomy has varied during the past few years. Thus, originally the second thoracic ganglion only was removed or cauterised. The operation has been extended caudally to include firstly the third thoracic ganglion and latterly the third and fourth ganglia. Telford's operation had been performed elsewhere on two extremities and in one case the third thoracic ganglion on both sides was removed instead of the second. Removal of the stellate ganglion with the second thoracic ganglion was performed on two patients at different clinics.

As seen in Table II., where removal of the stellate and second thoracic ganglia was undertaken, vasomotor tone remained absent. However, both of these sympathectomies were performed for conditions other than Raynaud's Phenomena. Both patients were sympathectomised some years previously, the operation being done thirty years previously in one subject.

Thirteen extremities were sympathectomised by removal or cauterisation of the second thoracic ganglion only. As judged by the plethysmographic observation, vasomotor tone was present in ten (77 percent.) instances. Three extremities in this group showed absence of vasomotor tone, i.e. sympathectomy is still complete. However, a return of symptoms has occurred in one subject, representing two extremities. Twelve of the thirteen extremities were sympathectomised for Raynaud's Phenomena, the remaining subject suffered from causalgia. It is this last patient that still has absence of vasomotor tone. Removal or cauterisation of the second thoracic ganglion in patients with Raynaud's Phenomena has not been successful in 100 percent. of cases, as judged by the plethysmographic method of determining vasomotor tone.

The second and third thoracic ganglia were removed in three extremities. Vasomotor tone has returned in two (both with Raynaud's Phenomena). The other patient also had

/Raynaud's

Raynaud's Phenomena but secondary to a cervical rib. Following removal of the rib and sympathectomy vasomotor tone is still absent. However, sympathectomy was undertaken only eighteen months previously.

Removal of the second, third and fourth thoracic ganglia had been done on eight extremities. Although return of vasomotor tone was apparent in only one extemity, the interval after operation is still too short for final assessment. Only six months had elapsed in most of the subjects examined and several of the tests were recorded within a month of operation. The subsequent history in one patient, however, notes that although Raynaud's Phenomena have not recurred, the extremities are colder than in the immediate post-operative period.

Telford's operation had been performed on both sides in one patient nine years previously. Vasomotor tone was present when re-examination took place.

The third thoracic ganglion was removed bilaterally in one subject. Vasomotor tone is present on re-examination three years later.

Therefore, as judged by the nature of sympathectomy, vasomotor tone is absent in only four cases with any degree of finality. Three cases represent non-vasospastic conditions, viz. causalgia, and of these, the stellate and second thoracic ganglia were removed in two and the second thoracic ganglion in one. One case of Raynaud's Phenomena associated with a cervical rib still has absence of vasomotor tone after removal of the second and third thoracic ganglia.

The remaining fourteen patients constituting twenty-six extremities are all sufferers of Raynaud's Phenomena and no matter what type of sympathectomy was performed either

/vasomotor

vasomotor tone has returned or the period after operation is not sufficient for definite assessment.

TABLE II.

Extent of Sympathectomy.	Number.	VASOMOTOR TONE. Present.	Absent.
Stellate and Th.2	2	0	2
Th.2	13	10	3
Th.2 and Th.3	3	2	1
Th.2, Th.3 and Th.4	8	1	7
Telford's Operation	2	2	0
Th.3	2	2	0

The time factor has been discussed already to a large extent. However, it is significant that in the first year after operation vasomotor tone has returned in 20 percent. of extremities examined. Of those extremities tested one or more years after operation, only four (21 percent.) still have absence of vasomotor tone. Of these four, Raynaud's Phenomena have been noted subjectively in two extremities. One extremity was sympathectomised for thrombo-angiits obliterans. Thus on a long-term basis only one (5 percent.) shows absence of vasomotor tone.

TABLE III.

Time after Operation	Number.	VASOMOTOR TONE. Present.	Absent.
0 - 12 months	10	2	8
1 - 10 years	19	15	4
Over 10 years	1	0	1

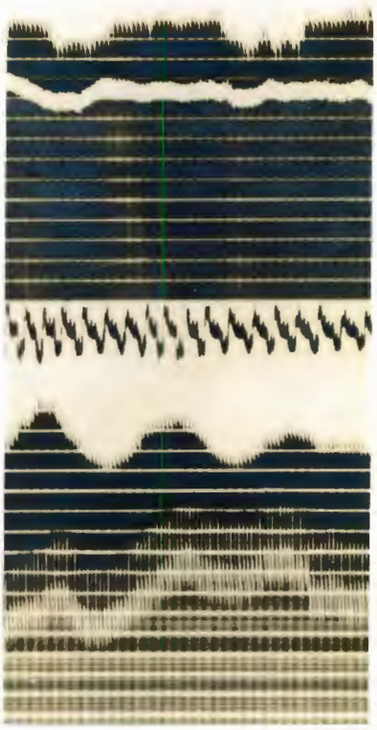


FIGURE 54.

Left Th.2, Th.3 and Th.4 removed twelve days previously.

The pulse volume of the left and right middle fingers at rest and after thirty minutes' body heating.

The left is the upper tracing in each case.

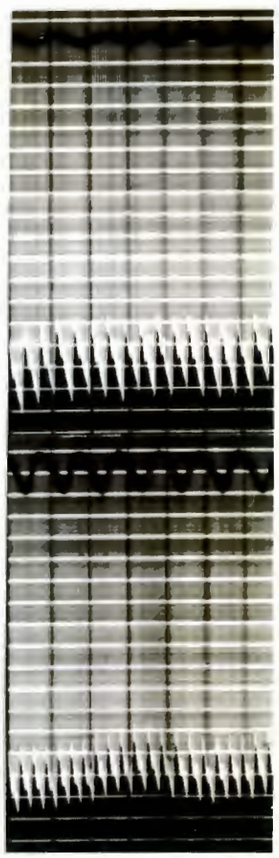
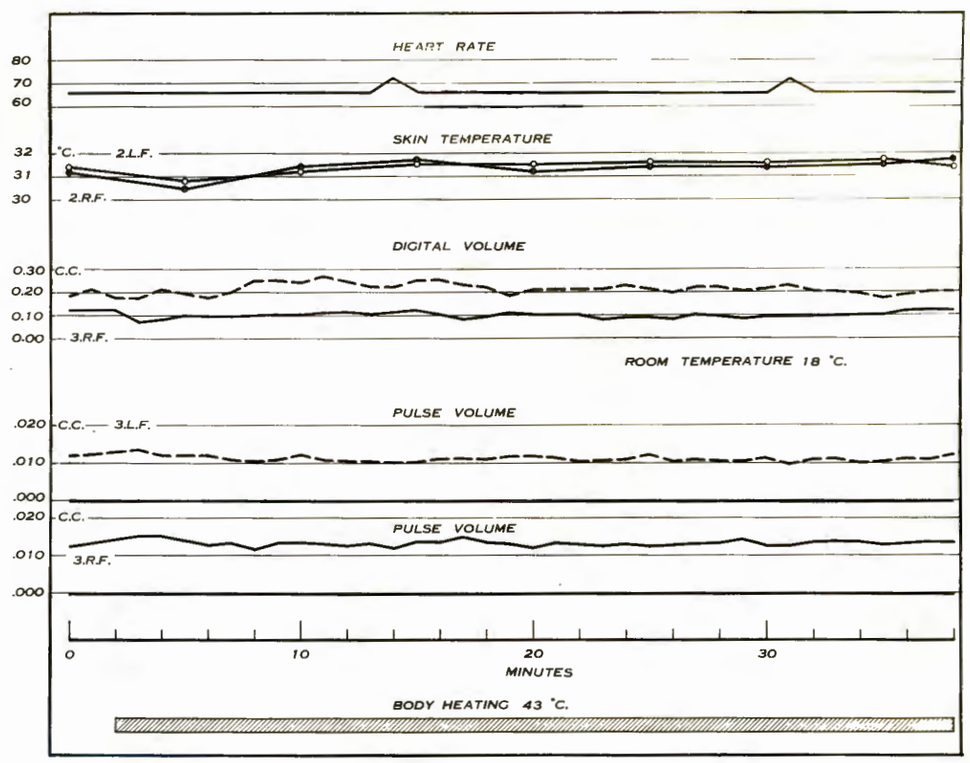


FIGURE 55.

Right Th.2, Th.3 and Th.4 removed five days previously.

The right middle finger at rest (upper) and after thirty minutes' body heating (lower).

Note the increase in pulse rate after heating.



GRAPH 25.

Same case as in Graph 9.

The effect of Body Heating -
nineteen days after removal of Right Th.2, Th.3 and Th.4,
and one month after removal of Left Th.2, Th.3 and Th.4.

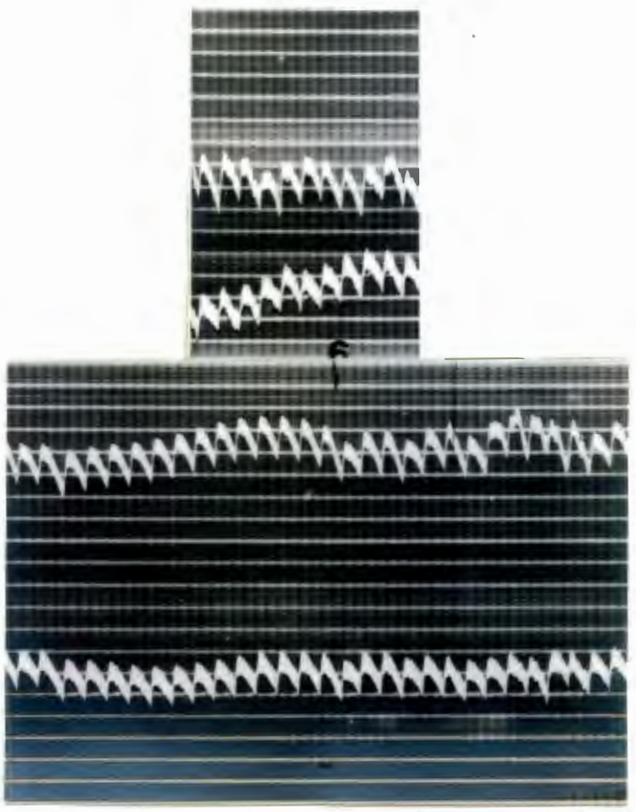
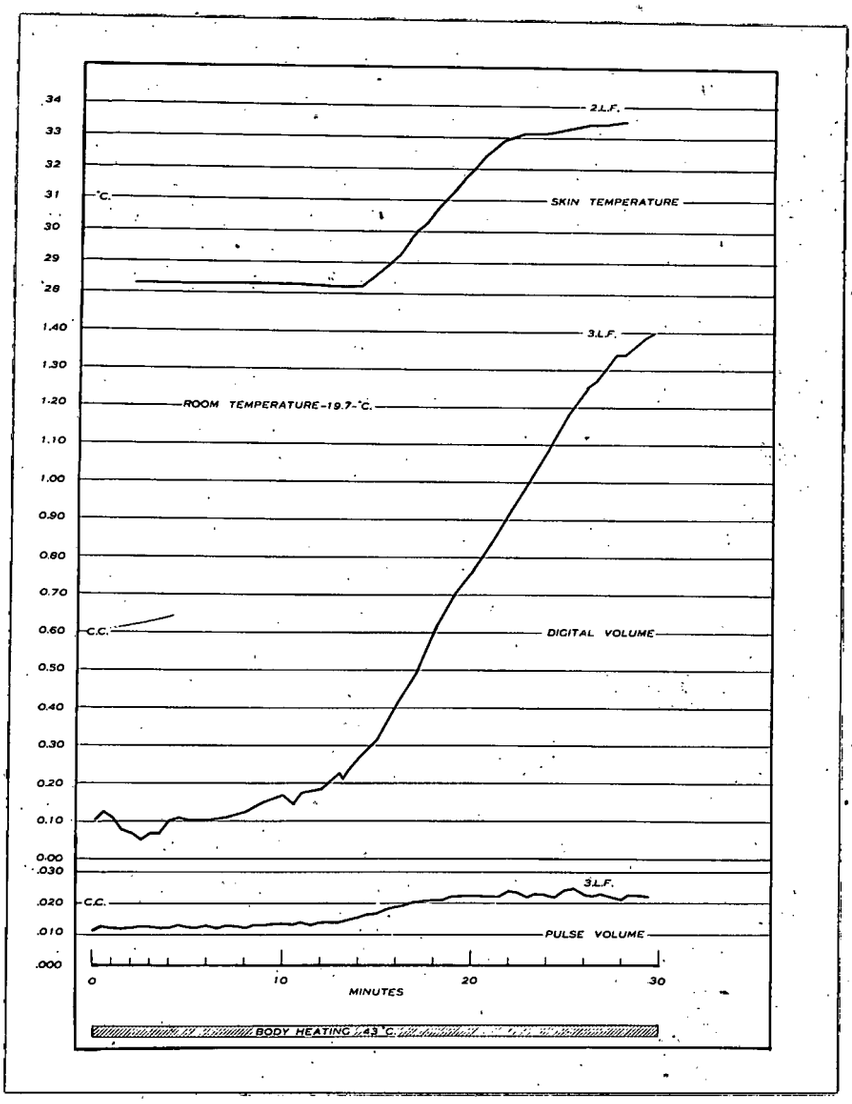


FIGURE 56.

Five weeks after removal of Left Th.2, Th.3 and Th.4
and nineteen days after removal of Right Th.2, Th.3 and Th.4.

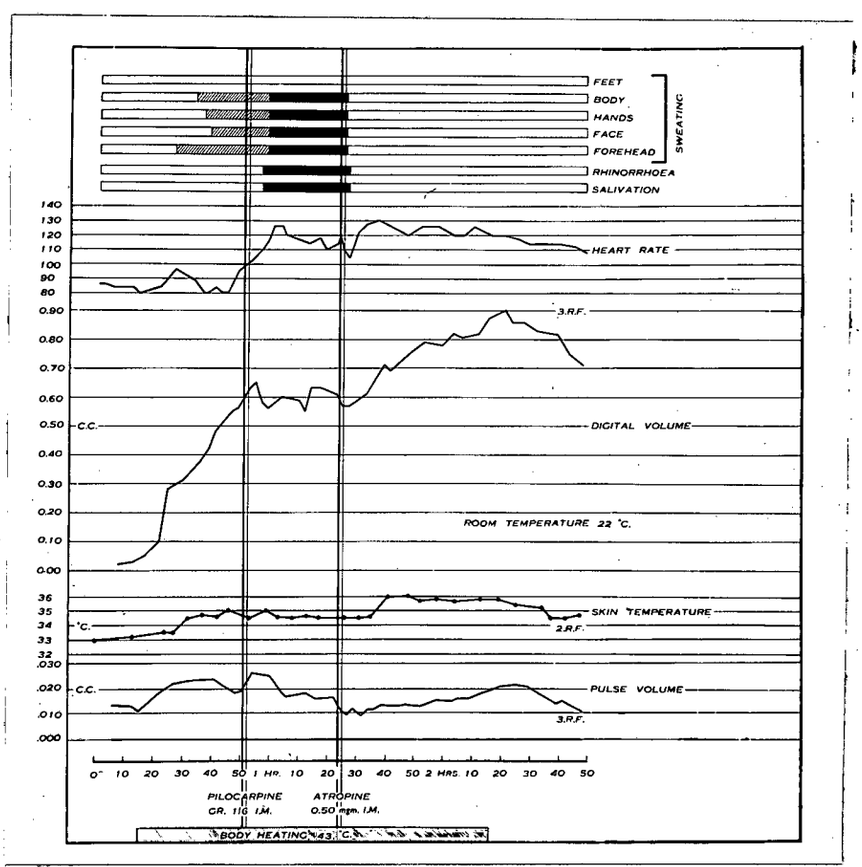
Left and right middle fingers at rest,
and after thirty minutes body heating.

The Left is the upper tracing in each case.



GRAPH 26.

The effect of body heating
three years after cauterisation of Left Th.2.

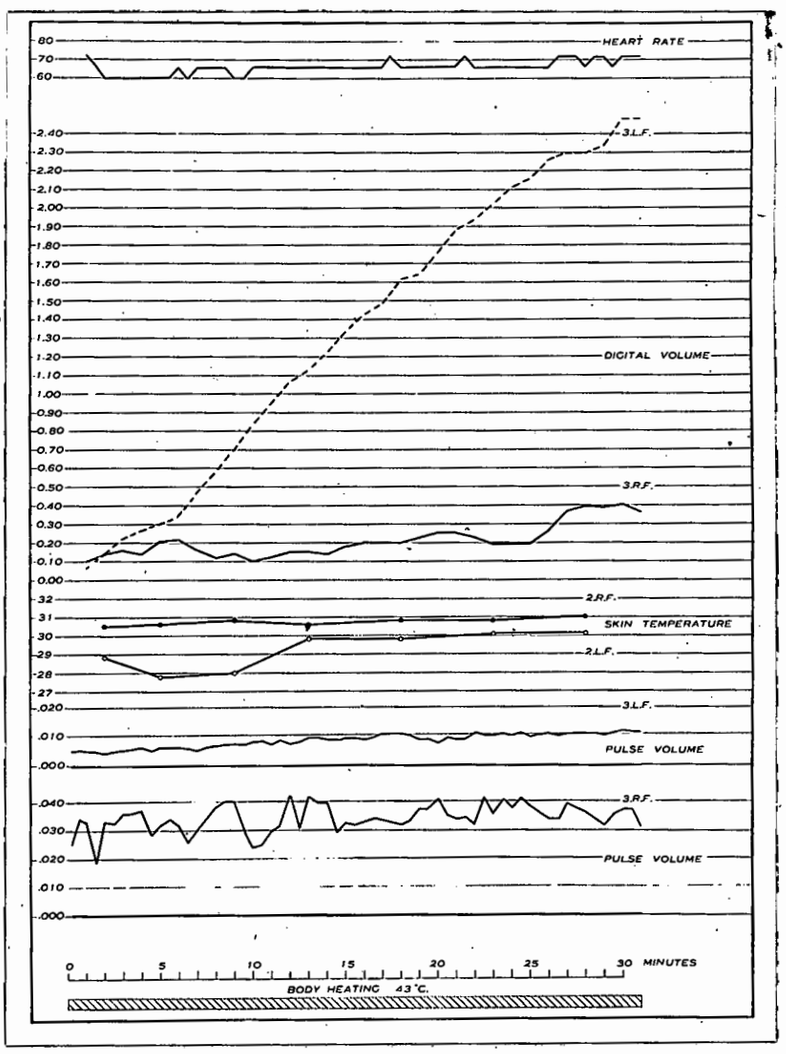


GRAPH 27.

Same case as in Graph 26.

Cauterisation of Right Th.2 three years previously.

Note the effect of body heating
before the administration of pilocarpine.



GRAPH 28.

The effect of body heating

Stellate and second thoracic ganglia removed thirty years previously.

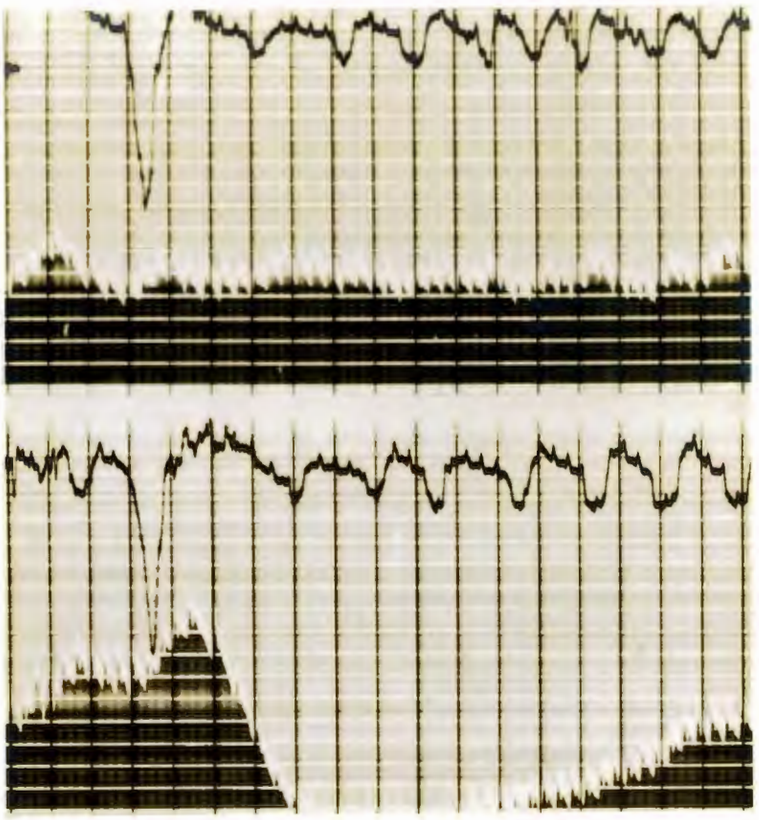


FIGURE 57.

The effect of a single deep breath on the sympathectomised left middle finger (upper tracing) and the normally innervated right middle finger.

Cauterisation of the Left Th.2 only was done.

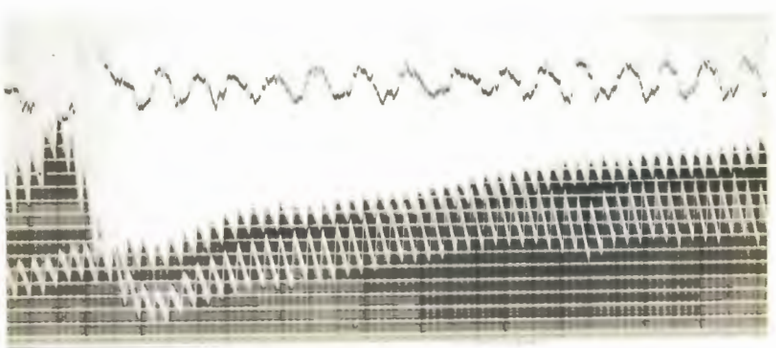


FIGURE 58.

The effect of a deep breath on the sympathectomised left middle finger and the normally innervated right middle finger recorded simultaneously.

Left stellate and second thoracic ganglia removed thirty years previously.

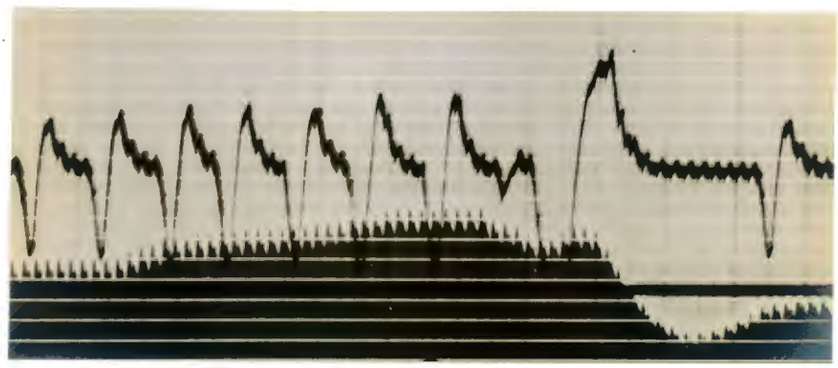


FIGURE 59.

The effect of the accidental recording of a sigh on the right middle finger

Three years after cauterisation of the right second thoracic ganglion.

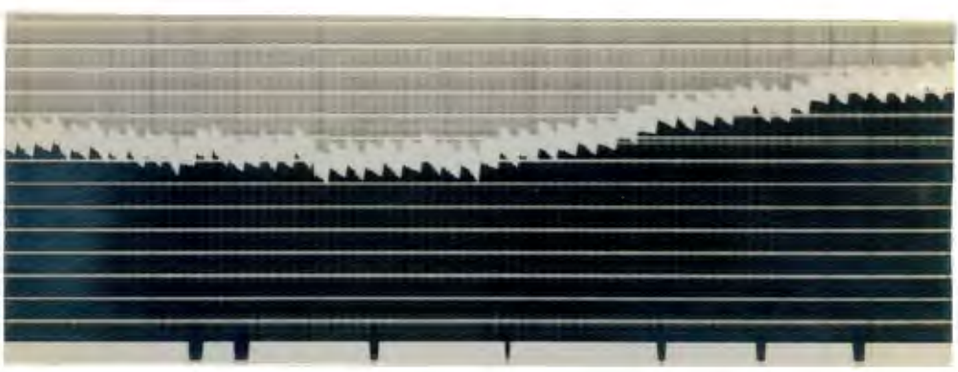


FIGURE 60.

The effect of multiple pinpricks on the Left middle finger.

Thirty years after stellatectomy and second thoracic ganglionectomy.

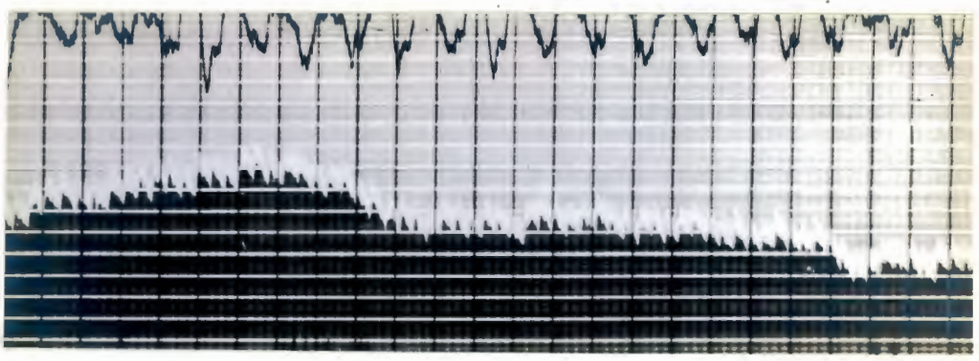


FIGURE 61.

The effect of multiple pinpricks.

One year after cauterisation of the Left second thoracic ganglion.

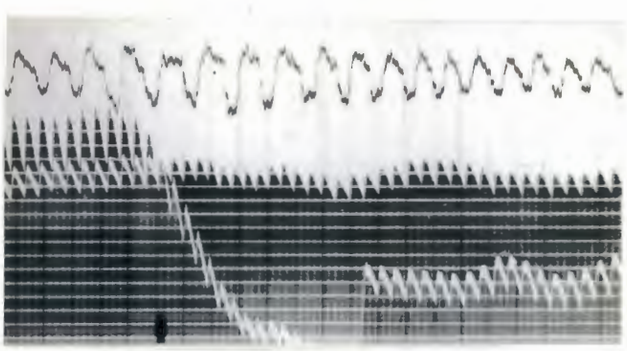


FIGURE 62.

The effect of applying ice to the feet i.e. reflex cold causing vasoconstriction.

Left stellatectomy performed thirty years previously.

Signal shows point of inserting feet into cold water.

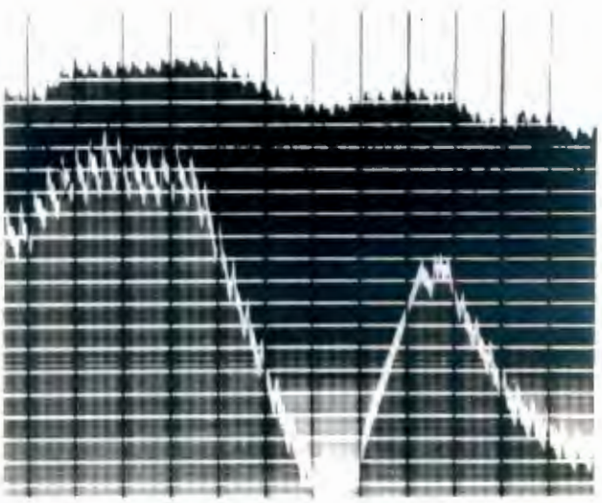


FIGURE 63.

The left middle finger (upper tracing)
and right middle finger.

Cauterisation of left Th.2 eighteen months previously.

The effect of immersing both feet in iced water.

(b) SUMMARY AND CONCLUSIONS.

In assessing the results of the investigations as a whole, the striking feature was the close agreement amongst the various tests. Although the tests may illustrate different aspects of sympathetic activity, correlation showed that there was uniformity throughout. Thus, there was close similarity in the denervated areas obtained from both the sweating and skin resistance tests. Similarly, where there was a return of sweating, the plethysmograph indicated return of vasomotor tone. Also vasoconstriction occurred in response to pilocarpine.

It was at once apparent that 90 percent of cases examined within twelve months of operation still showed sympathectomy to be complete. Those cases examined within six months of sympathectomy consistenly showed this feature.

The late results of sympathectomy of the upper extremity, however, showed a different picture. All tests indicated that there had been a return of both sudomotor and vasomotor functions in all.

In all cases of Raynaud's Phenomena the second thoracic ganglion was the upper limit of sympathectomy. The second thoracic or the second and third thoracic ganglia were removed or cauterised in those cases included as "late results", i.e. twelve months after sympathectomy. In these patients return of sudomotor and vasomotor functions had occurred.

The second, third and fourth thoracic ganglia were removed in the cases classified as "early". In these cases sudomotor activity and vasomotor tone were still absent. However, the period after sympathectomy is still too short to assess the results finally. As judged by the vasoconstriction caused by pilocarpine in two cases, it is likely

/that further study

that further study in these cases will reveal a return of vasomotor tone in the future.

Cauterisation via the thoracoscope was the method of sympathectomy in some cases. In others, dissection transpleurally was performed. The difficulties of the former procedure are greater and, therefore, exact localisation is more difficult. There is very little difference in the results of either method of sympathectomy. Anatomical abnormalities or the presence of adhesions combine to make errors more prevalent in cauterisation of the thoracic chain. Errors are less likely in open dissection of the ganglionated trunk.

The vasomotor and sudomotor changes after sympathectomy were noted in a case of thrombo-angiitis obliterans and in one case of causalgia in which stellatectomy had been done. In these two cases the sympathectomy was still complete nine and thirty years after operation.

(c) CASE HISTORIES.

Number 1.

Miss M. v.R., 42, white, female, was first seen in 1943 with a diagnosis of ?Raynaud's Phenomena of two years' duration.

Thoracic sympathectomy was performed, using the thoracoscope, on 21/1/44 (left) and on 17/2/44 (right). In each case the second thoracic ganglion only and its rami were cauterised.

In both instances the hands were warm and did not sweat immediately following operation.

Bilateral transperitoneal lumbar sympathectomy was performed on 9/3/44. L.2 and L.3 were removed on both sides.

Sweating tests done between and after operations revealed definite levels of anhidrosis. It is interesting to note that removal of the second thoracic ganglion did not result in a loss of sweating of the face and neck. The anhidrosis was confined to the upper limb and a band across the back. (Figure 23. - page 97).

Exactly three years later the patient was re-examined. Since operation she has never had a return of symptoms. The hands have remained warm throughout the coldest weather. The cyanotic colour changes have not recurred. She never experiences any pain or feeling of coldness. The hands have never sweated since operation. As far as she is concerned the operation has been 100 percent. successful. The results in the hands correspond exactly with those of the feet.

On examination at this time both hands and feet were warm. The colour of all four extremities was a pale pink. There were no changes in the textures or nature of the skin of the digits. No ulceration or trophic disturbances were seen. All the pulses were readily palpable.

Skin temperature recordings taken on 28/1/47 reveal high temperatures at rest. (Figure 64. - page 235). The recordings taken after immersion of both feet in a water bath at 45°C. for thirty-five minutes show no increase in skin temperatures.

Thermo-regulatory body heating was repeated two months later and again no appreciable increase in skin temperature occurred.

Graph 20. (page 197) shows the response of the digit to pilocarpine. Vasoconstriction occurs.

At rest the pulse volume of the right middle finger measures .01cc. (Figure 65. - page 235), whereas after thirty minutes thermo-regulatory body heating the pulse volume has increased to .02cc. (Figure 66. - page 236). The response to thermo-regulatory body heating is shown in Graph 26. (page 224).

/The response

The response of the pulse and digital volumes to a deep breath is shown in Figure 67. (page 236). Vasoconstriction occurs.

Three years after the second thoracic ganglion had been cauterised on both sides, the patient is completely satisfied with the sympathectomy. There has been no return of symptoms for which the sympathectomy was performed. Yet in spite of this subjective cure the evidence points to a return of sympathetic tone in the vessels of the upper limbs.

There is a dilatation of the vessels in response to reflex body heating. This can only occur where the sympathetic supply to the vessels is intact.

Further it is noted that on deep inspiration both the pulse volume and digital volume diminished, another factor dependent on the integrity of the sympathetic nerves to the vessels.

Pilocarpine nitrate acts as it does in the normal non-sympathectomised limb, producing a fall in the skin temperature.

The Starch-Iodine sweating test was inconclusive at first. Sweating was quite apparent in those places where it was not immediately after operation, i.e. on the forearms and, to a lesser extent, on the hands. Yet on the posterior aspect of the trunk the same line of demarcation is seen three years later as was noted after operation. Five months later, however, the line of demarcation had completely disappeared. Sweating was generalised over the whole extremity although small patches of anhidrosis are perceptible, particularly on the ulnar surfaces of the hands. (Figure 22. - 27., pages 96 - 100).

The skin resistance method shows the same patchy pattern as does the Starch-Iodine test. (Figures 46. and 47., pages 139 and 140).

Conclusions:

There is return of sympathetic innervation to both upper extremities.

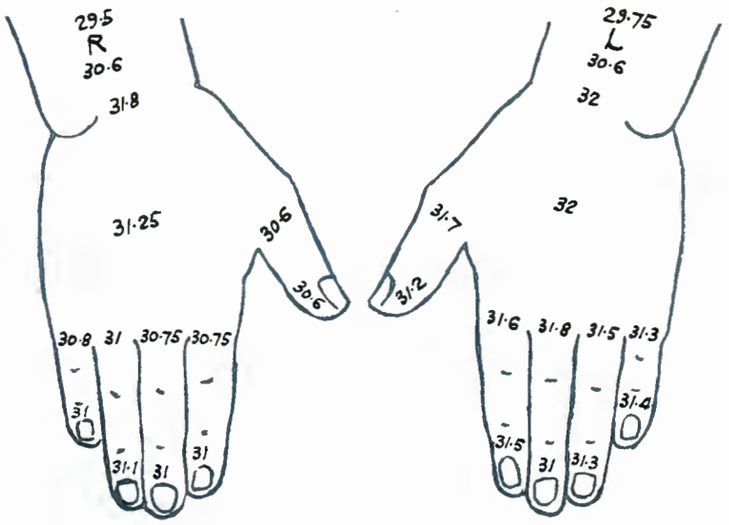


FIGURE 64. - CASE No. 1.

The skin temperatures of the digits at rest three years after bilateral cauterisation of the second thoracic ganglia.

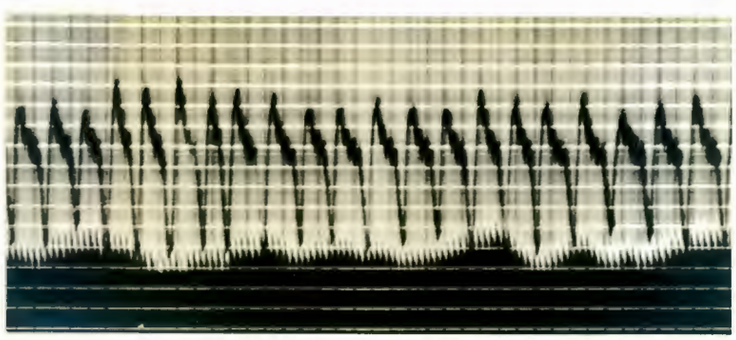


FIGURE 65. - CASE No. 1.

Right middle finger at rest.

Three years after cauterisation of the right second thoracic ganglion.

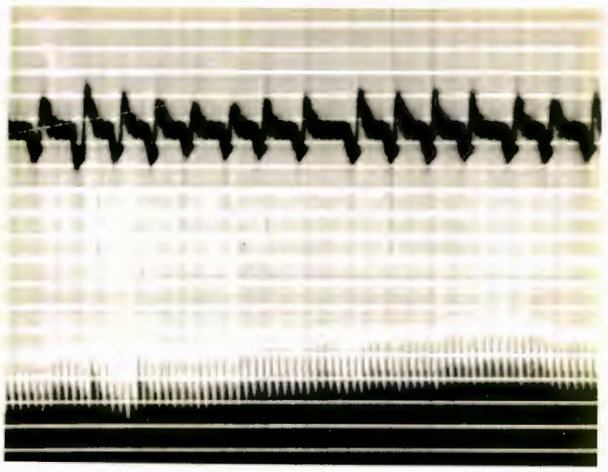


FIGURE 66. - CASE No. 1.

Right middle finger after thirty minutes body heating.

Three years after cauterisation of the right second thoracic ganglion.

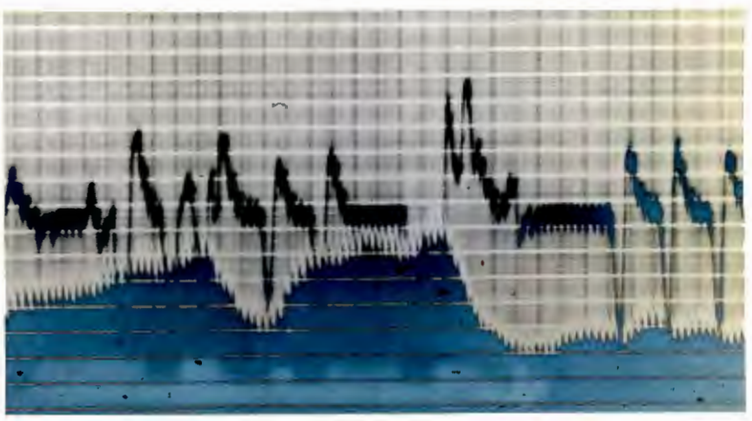


FIGURE 67. - CASE No. 1.

Right middle finger.

Note the effect of a deep breath.

Number 2.

Miss. W., 38, white, female, was first seen on 20/9/43. At that time she complained of numbness of the left fourth finger of about three months' duration. This was not associated with exposure to cold. It was accompanied by colour changes. At first the finger was yellow and, later, blue. The blueness remained for a variable period of a few minutes up to several hours and then disappeared.

The patient was noted to have rather cold hands. Nothing else of note was found locally except that all the peripheral pulses were easily felt. She was a rather nervous type and sweated easily.

The patient was judged to be a case of ?Raynaud's Phenomena. Accordingly, a bilateral thoracic sympathectomy was performed in two stages. In each the thoracoscope was used and the second thoracic ganglion cauterised. No complications developed. There was no Horner's Syndrome. The left ganglionectomy was performed on 2/3/44, and the right on 23/3/44.

On the day following operation on each side the sympathectomised limb was noted to be warm and dry.

Minor's Starch-Iodine sweating test was performed shortly after, at which it was noted that there was complete absence of sweating of both hands and arms, face and chest wall. Sweating was present in the axilla. A well-defined line of demarcation was present separating the sweating and non-sweating areas. (Figures 16. and 17. - page 90 and 91).

Five months after operation, on 23/8/44, the patient complained of numbness of the left arm. On one occasion, subsequent to operation, she noticed blueness of the left fourth finger after exposure to cold. Her hands had not sweated since operation.

She was referred to the consulting neurologist and was diagnosed as having "a highly nervous state."

The patient was next observed on 22/3/47. Throughout the three years following operation she had been somewhat improved. Her symptoms were more general than confined to the extremities. The symptoms referable to the hands had never been very severe. She had noticed that her hands had been warmer than before operation. They very seldom sweated. Since operation she sweated rather more on the body than previously.

Examination at this stage revealed dry, warm, pink hands. No evidence of trophic changes was present. There was no sign of scleroderma or sclerodactyly. General examination was negative.

Skin temperature recordings at rest are shown in Figure 68. (page 239). The hands were warm and dry. After thirty minutes thermo-regulatory body heating she sweated profusely on all areas of the body except the face and neck. Both upper limbs sweated profusely. At the

/same time

same time the skin temperatures had risen to the full dilatation level.

At rest the pulse volume of the left middle finger was just less than .01cc. After thirty minutes thermo-regulatory body heating the height of the pulse volume had risen to .015cc. (Figure 69. - page 240).

Minor's Starch-Iodine sweating test performed on 4/4/44 shows complete absence of sweating on both hands, face, neck and part of the chest anteriorly. The margin is well defined. The test was repeated three years later. Sweating as a result of thermo-regulatory body heating is seen to occur on both hands; no definite area of anhidrosis is seen. Sweating occurs on all areas previously dry. (Figure 18. - page 92).

The skin resistance was estimated. There was no apparent difference between the sympathectomised and normally innervated areas. (Figures 44. and 45. - pages 137 and 138).

It was apparent five months after bilateral cauterisation of the second thoracic ganglion that sympathectomy, as performed in this case, was not complete. Since that time there has been a complete return of sympathetic function in the two upper extremities. This is indicated by the following features:-

i. Subjective improvement has not been maintained.

ii. Thermo-regulatory body heating produces reflex sweating; the pulse volume rises from .01cc. to .015cc.

iii. Respiration changes the pulse volume.

iv. Pilocarpine causes vasoconstriction.

Conclusions:

There is return of sympathetic innervation of both upper extremities.

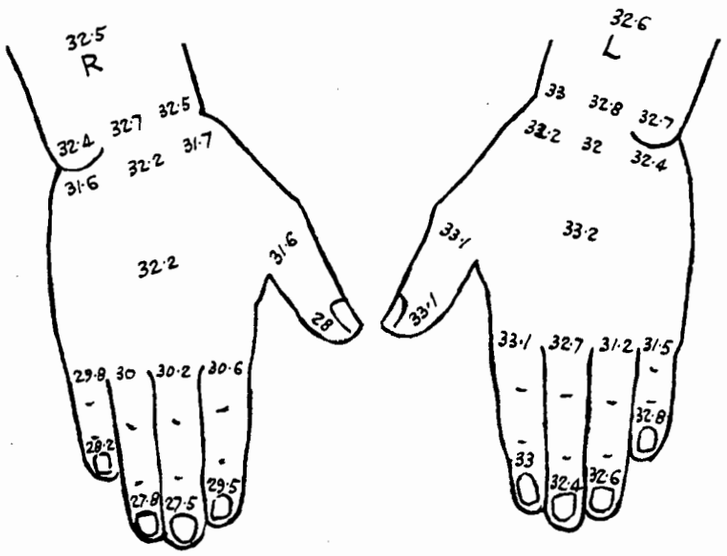


FIGURE 68. - CASE No. 2.

Skin temperatures of both hands.

Three years after cauterisation of Th.2 bilaterally.

Room temperature 25.5°C.

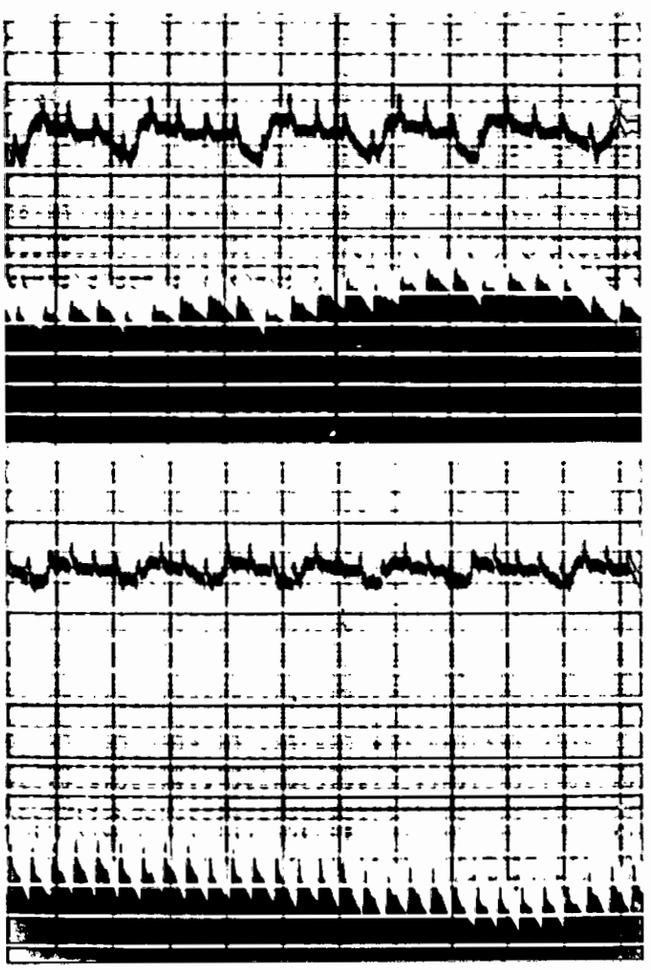


FIGURE 69. - CASE No. 2.

The left middle finger at rest and after body heating.

Three years after cauterisation of the second thoracic ganglion.

Note the increase in pulse volume.

Number 3.

Miss L., 45, white, female, first attended the peripheral vascular clinic on 21/11/43.

For the past twenty-two years she had noticed that her hands went dead in cold weather. There was no pain but "pins-and-needles". The fingers only were affected. On exposure to cold the fingers turned white followed by a purplish blue colour. On warming, her hands became a deep red. Paraesthesiae were felt in the stage of pallor. The attacks occurred during summer when exposed to strong wind. They were not brought on by mental or emotional strain.

She also complained of an epigastric pain, burning in nature. It had no relation to meals. She was nauseous on occasion but there was no association with the epigastric pain. No vomiting occurred.

She also complained of nervousness; was said to have a goitre when seventeen years old.

During winter she also suffered from chilblains of both hands and feet.

She was an extremely nervous individual. There was no suggestion of exophthalmos. She had a coarse tremor of the hands. No trophic or other changes were present in the skin.

There was a tachycardia of 100 beats per minute. Slight fullness of the neck was present.

All pulses in both hands and feet were easily palpable. The hands were cold and clammy.

A diagnosis of Raynaud's Phenomena was made and she was recommended for sympathectomy.

An adequate degree of collapse was obtained by artificial pneumothorax and on 18/7/44 the right second thoracic ganglion was cauterised via the thoracoscope. After operation the right hand and arm were much warmer than the left and there was no sweating on the limb or in the axilla, as compared with free sweating on the left side.

Repeated attempts to produce an artificial pneumothorax on the left side failed. Therefore, by open thoracotomy through the second interspace anteriorly the sympathetic chain was exposed. Many recent non-vascular adhesions were divided in the exposure. The second thoracic ganglion was defined and removed together with the intrathoracic ramus to the first thoracic nerve.

The left hand and arm were warm and showed no evidence of sweating after operation.

Minor's Starch-Iodine sweating test was performed on 20/2/45, i.e. nearly six months later. Sweating was present on both hands and forearms. Sweating was absent

/on the face

on the face, neck, shoulders and left upper arm. (Figure 19. - page 93).

Since operation there had been some improvement in that it is only the extremes of cold which bring on attacks. She was quite free from attacks during the summer. There had been no difference in the degree of sweating of the hands.

In March, 1947, skin temperature readings show a rise in response to thermo-regulatory body heating (Figures 70. and 71. - page 243).

The pulse volume of the left middle finger at rest on 26/3/47, i.e. nearly three years after sympathectomy, is .005cc. After thirty minutes thermo-regulatory body heating the pulse volume is .017cc. The corresponding figures for the right middle finger are .006cc. at rest, and .019cc. fully dilated. (Figures 72. and 73. - page 244).

Minor's Starch-Iodine test, repeated on 28/3/47 by means of thermo-regulatory body heating, showed sweating present in both hands, arms, shoulders and neck. Sweating was not brought out on the face with this method, but sweating was profuse thereon following pilocarpine. (Figure 20. - page 94).

The integrity of the sympathetic nerve supply to both upper extremities appears to be intact, according to the tests above. In each case the second thoracic ganglion was removed, the right by cautery, the left by open dissection. Although both hands were warm and dry immediately after operation, a sweating test, performed thirty-one weeks after the first operation, revealed sweating present in both hands.

Conclusions:

It is possible that sympathetic control of the upper extremities in this case had been re-established six months after operation.

Three years later there is little evidence to indicate that a sympathectomy had been done.

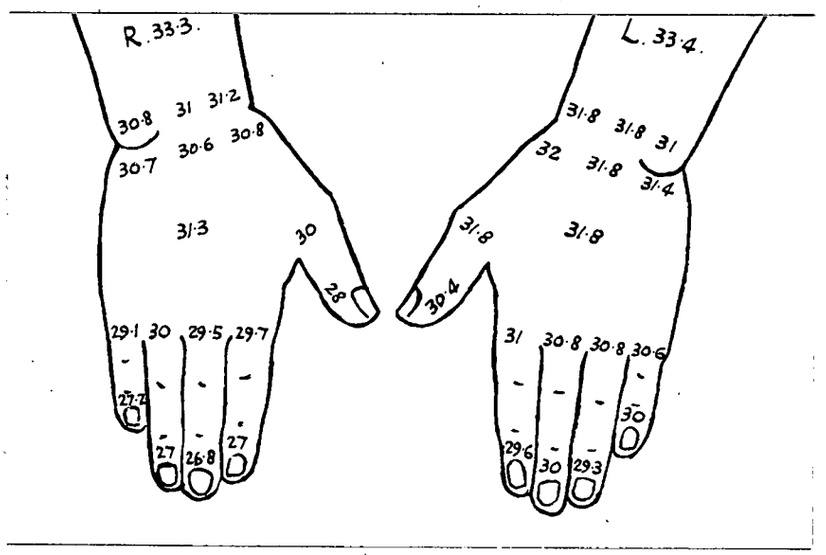


FIGURE 70. - CASE No. 3.

The skin temperatures of both hands at rest.

Three years after cauterisation of the right second thoracic ganglion and removal of the left.

Room temperature 19.9°C.

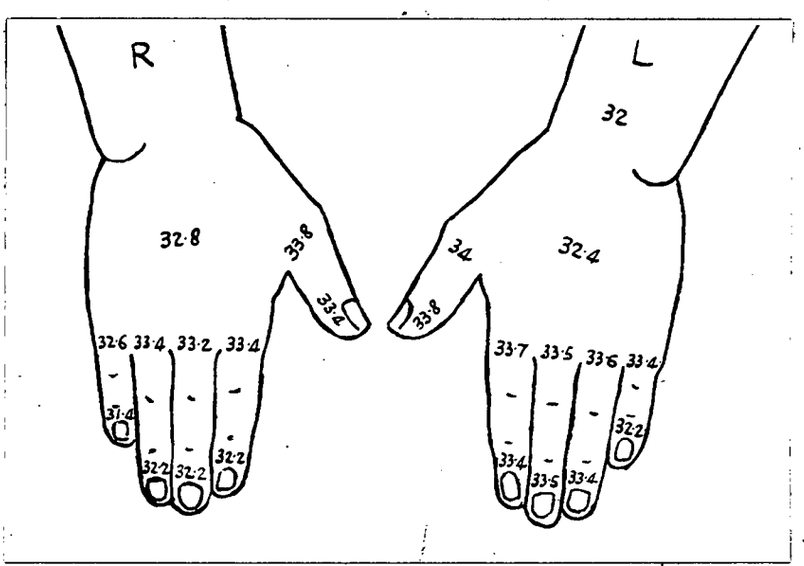


FIGURE 71. - CASE No. 3.

Skin temperatures after body heating.

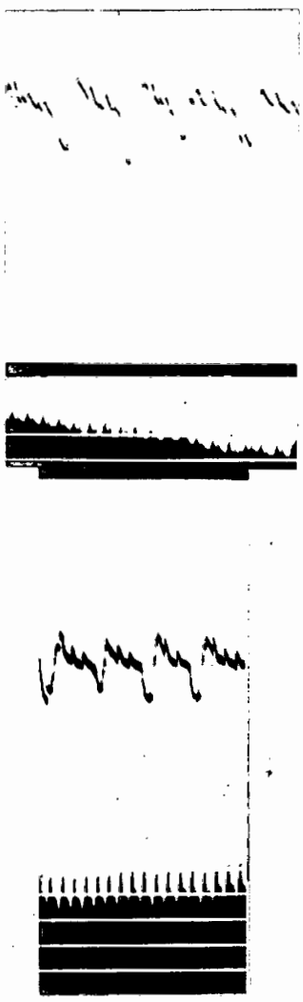


FIGURE 72. - CASE No. 3.

The left middle finger at rest and after body heating.

Note the change in pulse volume.

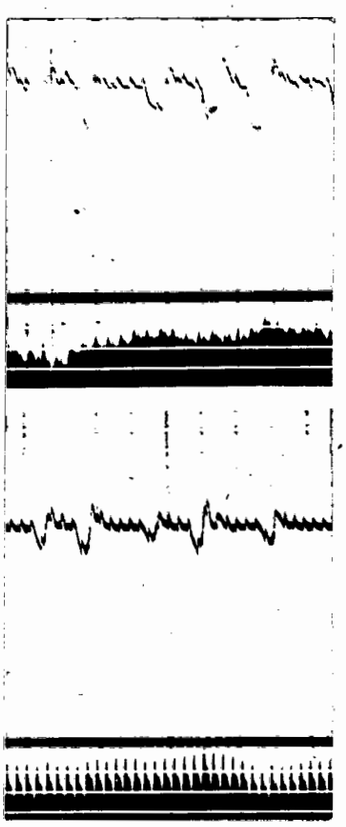


FIGURE 73. - CASE No.3.

The right middle finger at rest and after body heating.

Note the change in pulse volume.

Number 4.

Miss D.M., 33, white, female, was first seen in 1943. At that time her history went back fourteen years. During the winter months, on exposure to cold, her hands became white in colour. The fingers mainly were affected but the colour changes extended to the wrists. On very cold days when she arrived at work, her fingers were blue and stiff, and some time elapsed before normality was reached. During the warm summer months she was not affected in this way.

Her feet were similarly involved but did not incapacitate her to the same extent.

She also suffered severely from chilblains during the winter months. Ulceration occurred not infrequently, but healed rapidly with the onset of warmer weather.

She was easily depressed and always felt tired.

On occasion she has had "bilious attacks". These had been more frequent just prior to admission.

Examination revealed that this patient was suffering from Raynaud's Phenomena. The skin of her face was slightly thickened and she had rather expressionless features. It was felt that the cutaneous changes were those of early scleroderma, and the combination of Raynaud's Phenomena, scleroderma and a history of gastro-intestinal disturbances suggested the diagnosis of progressive systemic sclerosis. Complete radiological investigation of the gastro-intestinal tract, however, was negative.

When tested between attacks, the skin temperatures and the blood flow were all markedly below normal. There was hardly any pulse volume registrable even between attacks, and after the application of cold, there was complete arrest of the circulation.

When fully dilated, the skin temperatures reached the normal vasodilatation level and the pulse volume reached .018cc.

Capillary microscopy did not reveal any marked abnormality. Most of the loops were normal, only very few being slightly distorted and dilated.

Preganglionic ramisection was the treatment suggested.

Accordingly, on 9/6/43 a bilateral lumbar sympathectomy was performed transperitoneally, L.2 to L.4 being removed on each side.

On 18/8/43 a midline incision extending from the sixth cervical to the third thoracic spinous process was made with a view to removing both second thoracic ganglia and their rami. Part of the right first rib and transverse process of the first thoracic vertebra were removed and the sympathetic chain identified. The rami of the second thoracic ganglion were divided and the ganglion removed. The left side was not touched at this stage.

/On 23/9/43

On 23/9/43 the left second thoracic ganglion and its rami were removed via an incision in the second interspace anteriorly. Some oozing was noted and controlled. Post-operatively, however, massive pleural effusion developed which, with treatment, only resolved after eight weeks.

Immediately after operation the hands were warm and pink. Immersion into ice or cold water did not produce any Raynaud's Phenomena.

The upper extremities were considered to be completely sympathectomised.

Considerable improvement in her clinical state has resulted. Except for the last few months her hands have been warm. She has always noticed that the left hand appears somewhat warmer than the right. Her feet have been perfect and seem to be slightly warmer than the hands.

Depression, tiredness, and bilious attacks have not recurred. She had put on twenty pounds in weight.

She has noticed no change in the skin of her face since the operations.

Her hands and feet have been free from any sweating. She sweats excessively on the abdomen and back since sympathectomy.

When re-examined on 28/5/47 her hands were pink, but cold. Her feet were warm. There had been no change in her facial appearance. Both feet and hands were not sweating.

Skin temperatures of the hands were recorded at rest (Figure 74. - page 248), and after thirty minutes' body heating (Figure 75. - page 248). From a resting 22 - 23°C. the temperature rose to 33°C.

Plethysmographic records of the right fourth finger were taken at rest and after dilatation by thermo-regulatory body heating. The pulse volume, at rest, is again barely registrable and the rate of blood flow poor. At full dilatation the pulse volume reached 0.018cc. (Figure 76. - page 249). Similar change occurred in the left middle finger (Figure 77. - page 250) and the left big toe. (Figure 78. - page 251).

Minor's Starch-Iodine sweating test revealed sweating to be present on both upper extremities following thermo-regulatory body heating. Although patchy, there seems to be definite areas of anhidrosis. (Figure 21. - page 95).

Estimation of the skin resistance confirms this. (Figures 48. and 49. - pages 141 and 142).

Sweating in response to pilocarpine occurred all over the body and covered the whole of the upper extremities. There was no fall in skin temperature or pulse volume as these were low at the onset.

/The striking

The striking feature of this patient is the marked subjective improvement. Four years after preganglionic sympathectomy the patient is completely free of her pre-operative complaints.

Yet the state of the vessels appears to be unchanged from that before preganglionic sympathectomy was undertaken. The pulse volume at rest was barely registrable and after full dilatation the pulse volume rose to a figure identical to that obtained before operation, viz. 0.018cc.

Sweating tests indicate that reflex control of the sweat glands has been regained in a patchy and irregular manner. This is borne out by the skin resistance test which shows that the areas of high resistance are irregular in arrangement and appear to correspond with the Minor's Starch-Iodine test.

Injection of pilocarpine in this patient did not produce any vasoconstriction. This, in all probability, is due to the fact that the vessels at the time of administration were already in a state of constriction. It is, however, worthy of note that no vasodilatation occurred.

Sweating, as induced by pilocarpine, resulted in both sympathectomised and non-sympathectomised areas alike.

Conclusions:

There has been return of sympathetic innervation of the upper extremities in the patient.

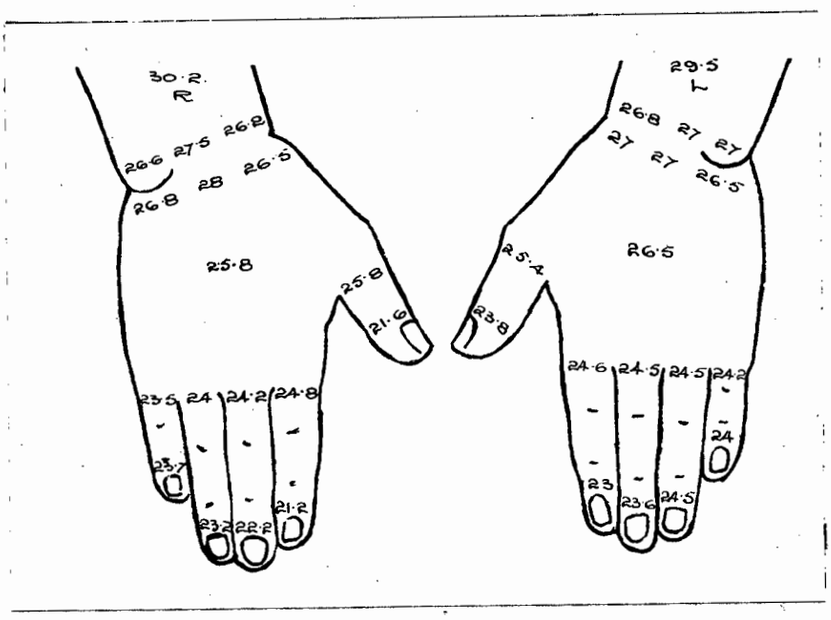


FIGURE 74. - CASE No. 4.

Skin temperatures of hands at rest.

Four years after bilateral removal of the second thoracic ganglion.

Room temperature 19.6°C.

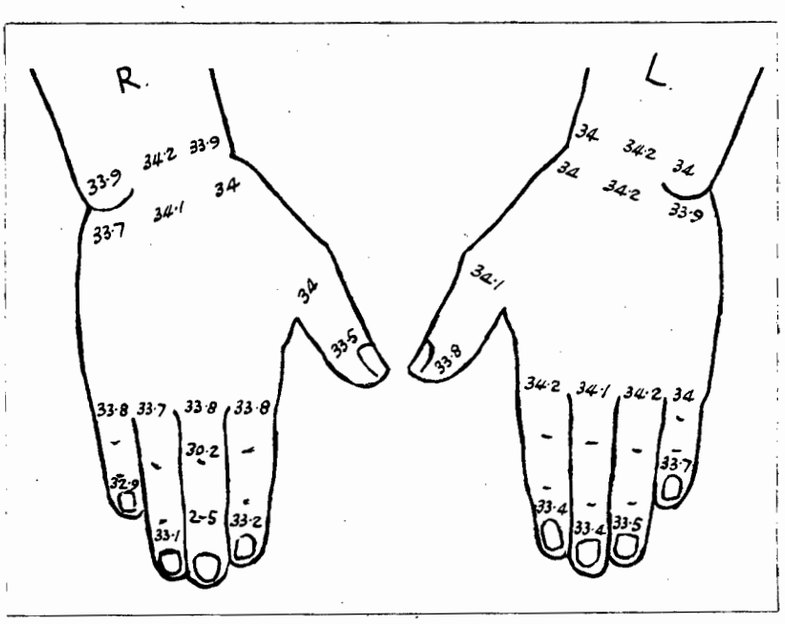


FIGURE 75. - CASE No. 4.

Skin temperatures of the hands after thirty minutes' body heating.

Room temperature 19.6°C.

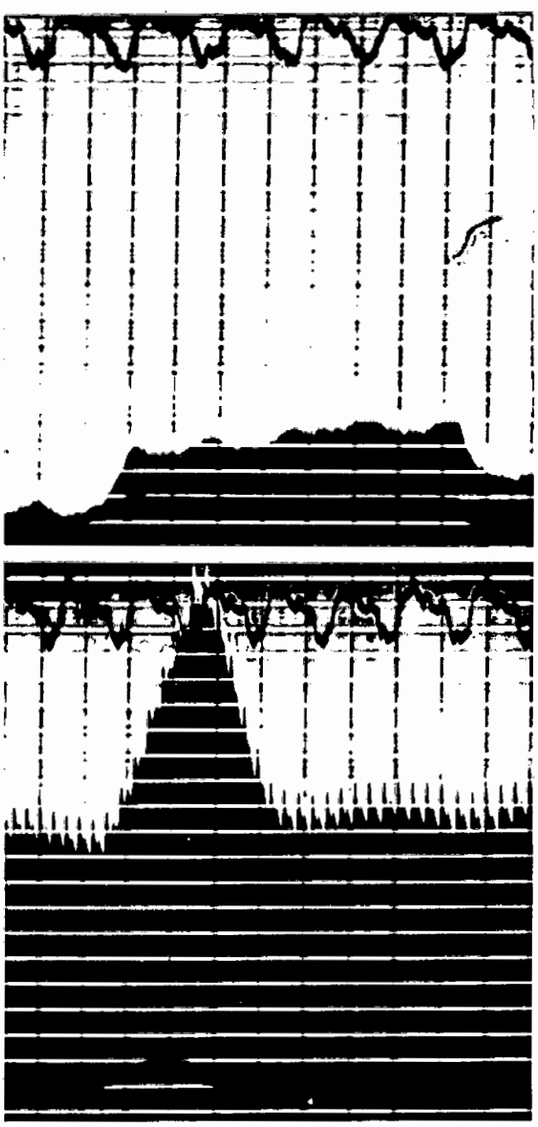


FIGURE 76. - CASE No. 4.

Right fourth finger at rest (upper tracing) and after thirty minutes' body heating.

Removal of Th.2 four years previously.

Note the increase in pulse volume and the change in rate of blood flow in response to a venous pressure of 60mm. Hg.

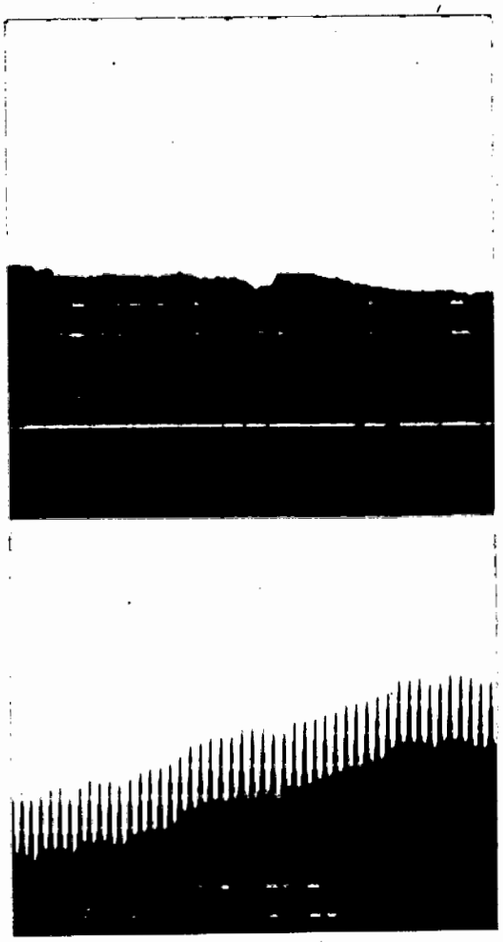


FIGURE 77. - CASE No. 4.

Left middle finger at rest (upper tracing) and after thirty minutes' body heating.

Removal of Th.2 four years previously.

Note the increase in pulse volume.

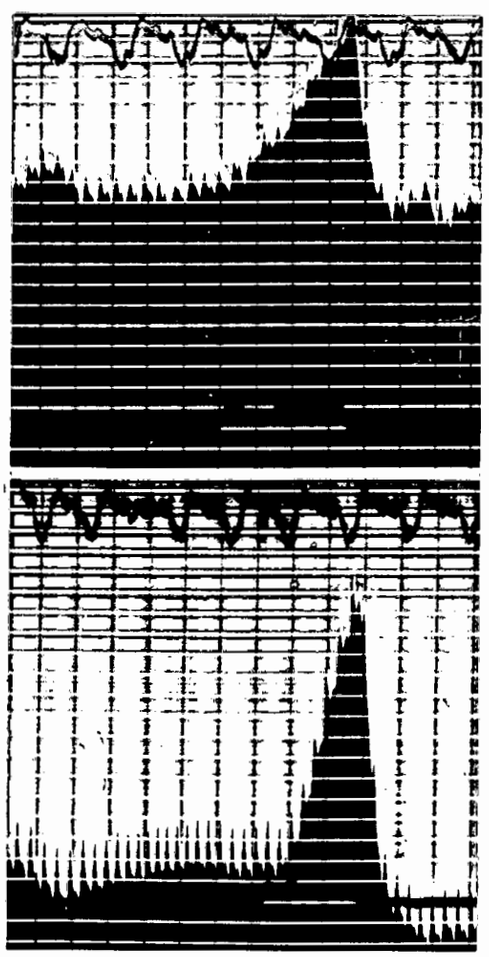


FIGURE 78. - CASE No. 4.

Left big toe at rest (upper tracing) and after thirty minutes' body heating.

L.2 to L.4 removed four years previously.

Note the increase in pulse volume and increase in rate of blood flow (pressure 60mm. Hg.).

Number 5.

Miss M.H., 44, white, female, had had "dead fingers" for as long as she could remember. No matter what clothes she wore her fingers turned cold and blue every time she left the house. Numberous physiotherapeutic measures were advised and tried without any improvement. At one institution ganglionectomy was suggested but not carried out.

She was seen by Sir Thomas Lewis. In London, it was noted that she had had Raynaud's Phenomena all her life. The attacks were frequent in cool or cold weather. Discolouration was present to the bases of the fingers, the hands were clammy; there was perfect mobility of the skin of the fingers and no scars were observed.

Right sympathectomy was performed on 24/5/38. Her notes report that: "Telford's operation, i.e. section below the third right ganglion" was the method employed.

Left sympathectomy was performed on 16/6/38. The result clinically was equally as good as that on the right. On 16/9/38 the patient reported that her hands were keeping as warm as when she left hospital.

"A little droop persisted of the left upper eyelid. She spoke of having acquired free perspiration from the waist down (abdominal sympathetics were untouched).

"In January, 1939, Sir Thomas Lewis heard indirectly that 'her hands still keep warm'."

After the operation she did not have attacks for about one year.

However, the first winter thereafter the attacks slowly came back. It first started in one finger of the right hand, then the others followed and within one year all fingers showed attacks again.

In 1942 it was noted that the left hand was also showing attacks. When watering the garden, even on a warm day, she had attacks. The attacks developed particularly when the temperature was below 67°F. Excitement never produced an attack, but when excited, cold produced an attack more easily.

Since operation she had noticed that, whereas before her nose used to turn blue, this had disappeared completely.

On 18/5/42 it was noted that the right hand was perspiring freely whereas the left hand was damp.

Her condition remained unchanged for the last five years, certainly as far as the hands were concerned. She had numerous other complaints, each of which had been completely investigated and no organic lesion noted. She had to nurse her father, aged 96.

A psychoneurotic element played a part in her numerous complaints.

/On 25/7/47

On 25/7/47 sweating was present in both axillae. The hands felt cold but were pink in colour. There was no evidence of pallor or blueness.

Skin temperatures of both hands showed that the left was 2°C. higher than the right. The left thumb registered 33°C. - about 6 - 7°C. higher than the other digits. (Figure 79. - page 254).

After thirty minutes' body heating the temperature of both hands reached full dilatation level. No difference was apparent in the two hands. (Figure 80.- page 254).

Sweating was present on both hands, forearms and arms, although the amount on the left appeared to be less. No sweating was observed on the face, neck and upper part of the chest. Sweating was profuse below this level.

Minor's Starch-Iodine sweating test confirmed this observation. (Figures 14. and 15. - page 88 and 89).

The skin resistance test also provided confirmation. (Figures 50. and 51. - pages 143 and 144).

On 12/8/47 the pulse volume of both hands was simultaneously recorded on the plethysmograph. The middle finger was used in each case. The pulse volume on the right side at the onset of the test was 0.003cc., and on the left 0.004cc. (Figure 81. - page 255).

Sweating in response to pilocarpine occurred on both upper extremities. The face, neck and shoulders, however, did not sweat at all. This corresponded with the areas of anhidrosis found with the Starch-Iodine sweating test.

On the administration of pilocarpine, both hands being fully dilated, first dilatation and then vasoconstriction occurred. (Figure 82. - page 255 and Graph 22. - page 190).

Conclusions:

Subjectively, therefore, Raynaud's Phenomena have returned. Objectively, there has been return of vasomotor and sudomotor functions. However, it is worthy of note that the Horner's Syndrome persists.

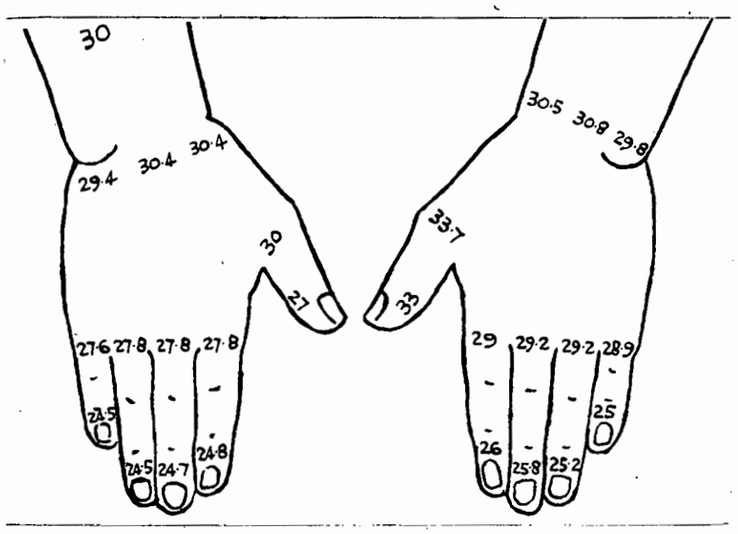


FIGURE 79. - CASE No. 5.

Skin temperatures of both hands at rest.

Nine years after bilateral Telford's operation.

Room temperature 21°C.

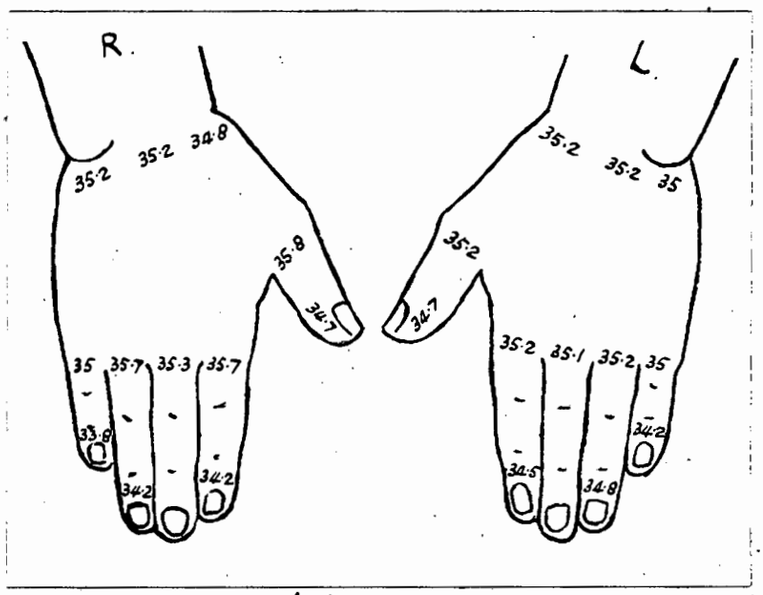


FIGURE 80. - CASE No. 5.

Skin temperatures of both hands after thirty minutes' body heating.

Room temperature 21°C.

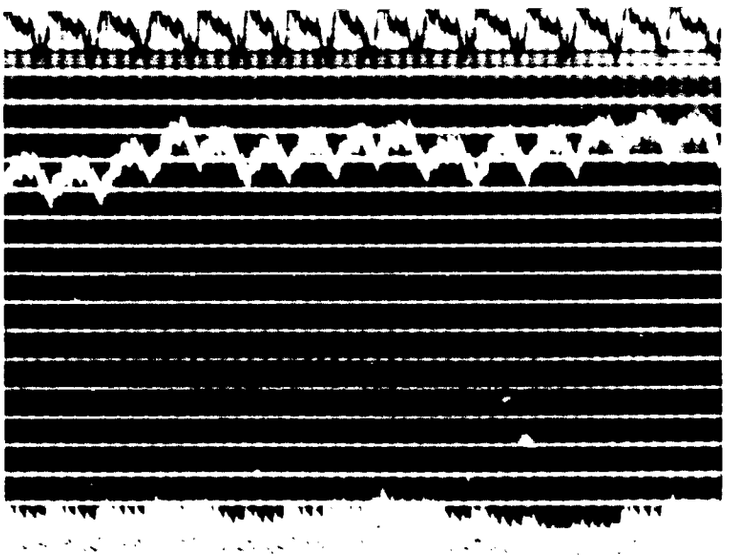


FIGURE 81. - CASE No. 5.

Right middle finger (upper tracing) and left middle finger at rest.

Bilateral Telford's operation nine years previously.

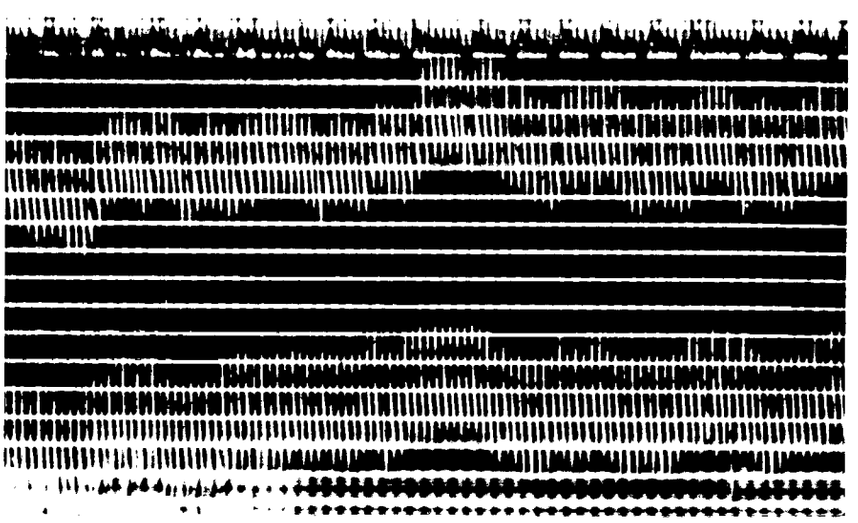


FIGURE 82. - CASE No. 5.

Right middle finger (upper tracing) and left middle finger twelve minutes after pilocarpine.

Number 6.

Mrs. O.L., 33, white, female, was first seen on 6/11/44. She complained of attacks of coldness and blueness of the hands and feet for the previous nine years. The attacks were brought on by cold weather and lasted from a few hours to a few days. The attacks were relieved by the application of warmth to the hands. The hands were affected rather more than the feet.

Examination revealed a mentally retarded individual with practically continuous attacks of Raynaud's Phenomena. No ulceration was present on the fingers. There was no evidence of scleroderma.

Plethysmography revealed a marked degree of spasm easily relieved by reflex body heating. No organic change was demonstrable plethysmographically.

On 6/12/44 the right second thoracic ganglion was cauterised via the thoracoscope. Immediately after cauterisation the right hand became warm and pink.

One week later the hand was still warm whereas the left hand was noted to be cold and blue.

Cauterisation of the left second thoracic ganglion was attempted subsequently but considerable difficulty was encountered from numerous vascular adhesions. Accordingly, the ganglion was extirpated by open thoracotomy.

Bilateral lumbar sympathectomy was performed on 20/2/45.

Minor's Starch-Iodine sweating test was performed shortly after. Patchy areas of sweating were seen over the face and neck. Sweating appeared diminished over the arms, but it was not completely absent. The result of sympathectomy on sweating was less effective on the left side.

The patient was discharged from hospital on 11/3/45. She reported again on 6/1/48.

Following lumbar sympathectomy her feet have always been warm. She has never had any recurrence in the lower extremities.

On 12/3/45, on reaching home, her hands were blue and cold. The hands sweated again shortly afterwards. For a short while, in spite of the return of symptoms, some improvement was obvious. The attacks did not come on as frequently, nor did they last as long. Also the fingers did not feel so "dead".

During the last six months, however, the attacks have been as severe as before operation. Exposure to cold brings on an attack, as does any emotional disturbance. During winter the hands are continually cold and blue.

She also has had several attacks of hallucinations and confusion. One such episode was actually observed in

/hospital

hospital and was considered to be possibly cerebral Raynaud's Phenomena.

On examination her hands were continually blue and cold. This was in marked contrast to the warm, pink, dry feet.

Plethysmography revealed a marked degree of spasm (Figure 83. - page 259), which could easily be relieved by reflex body heating. The spasm spontaneously resolved on several occasions. (Figure 84. - page 259).

In view of the return of symptoms it was decided to remove the stellate and middle cervical ganglia. On 5/2/48 the stellate ganglion was exposed on the left side. Telford's approach was used and, after division of the scalenus anterior, the ganglion was easily defined.

The sympathetic trunk was traced downwards from the stellate by stripping the pleura. The latter was easily reflected past the second rib to the lower border of the third rib. Here the pleura was firmly adherent and could not be separated. At this point the sympathetic trunk disappeared into a mass of fibrous tissue.

The sympathetic trunk was divided at this level and the second thoracic ganglion freed of all its connections. The sympathetic chain above the stellate was dissected cranially to define the middle cervical ganglion. The whole piece, i.e. second thoracic, stellate and middle cervical ganglia was then removed.

It is of interest that the subclavian artery became thread-like at the slightest touch, so intense was the spasm. After sympathectomy the spasm was relieved.

The following day a distinct difference was present between the two sides. The left side of the face was pink and dry. There was ptosis of the left upper lid and the pupil was smaller than the right.

The left hand was warm, dry and pink. There was no evidence of Raynaud's Phenomena, in marked contradistinction to the right hand which was blue and cold.

Six days later Raynaud's Phenomena were still present in the right hand. The left hand was still warm and pink. No sweating was observed on the left side of the face or left hand.

On 19/2/48 the right stellate ganglion was exposed in the same way. On this side, too, the pleura was separated from the posterior aspect of the thoracic cage. Reflection was relatively simple up to the third rib. Again difficulty was encountered at this point on account of thick fibrous tissue. The intact second thoracic ganglion was removed together with the stellate. On this side the middle cervical ganglion was not defined.

The following day there was no evidence of Raynaud's Phenomena on either side. Both hands and both sides of the face did not sweat. The pupils were equal and no apparent difference could be observed between the eyes.

/on the sixth

On the sixth post-operative day it was noticed that the Horner's Syndrome was less marked on the right side. Ptosis was less and the right pupil was larger than the left.

The patient was discharged from hospital three weeks later. Sympathectomy appeared complete. The skin of the face was dry and appeared looser and more elastic than on admission. No Raynaud's Phenomena had occurred in either hand.

This patient presented over three years previously with Raynaud's Phenomena of the hands and feet. Bilateral lumbar sympathectomy resulted in complete cure. There had been no return of symptoms over three years after operation. Sympathectomy was so far complete and permanent.

The upper extremities, however, presented a different picture. "Sympathectomy" was undertaken on both limbs. Whereas cauterisation was considered successful on the right upper limb, an attempt to cauterise the left second thoracic ganglion was abandoned because of dense adhesions. The thorax was, therefore, opened and the ganglion removed transpleurally under direct vision.

Post-operatively no Raynaud's Phenomena were observed for one month. The patient was discharged from hospital and the following day Raynaud's Phenomena appeared in the hands.

Sweating tests prior to discharge, whilst showing considerable diminution, did not reveal the expected complete absence of sweating. At this early stage, therefore, it was probable that sympathectomy was not complete.

The subsequent progress of the case confirmed this assumption. Raynaud's Phenomena recurred and for a short while the patient observed that there was some improvement. At the time of re-examination, however, Raynaud's Phenomena were continually present.

Plethysmography, sweating tests and the response to pilocarpine all confirmed, that, whatever had been removed originally, sympathectic innervation to both upper extremities was still intact.

Re-operation was, therefore, carried out. On each side the second thoracic ganglion was found to be present. It appeared that the third thoracic ganglion was mistakenly removed for the second on both sides.

In this patient, therefore, recurrence of Raynaud's Phenomena was not due to regeneration of the sympathetic but to incompleteness of the sympathectomy. That this was so could be surmised from the early and complete return of symptoms.

By removal of the stellate and second thoracic ganglia together with the intervening trunk on both sides, and of the middle cervical ganglion on the left, it is hoped that sympathectomy is complete now.

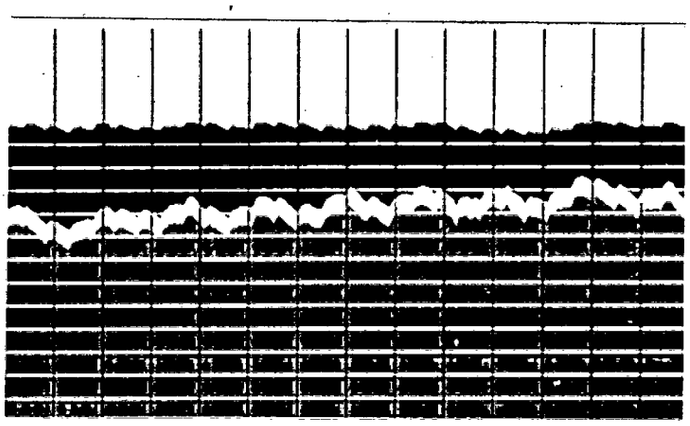


FIGURE 83. - CASE No. 6.

Left middle finger (upper tracing) and right middle finger.

Three years after bilateral removal Third thoracic ganglion.

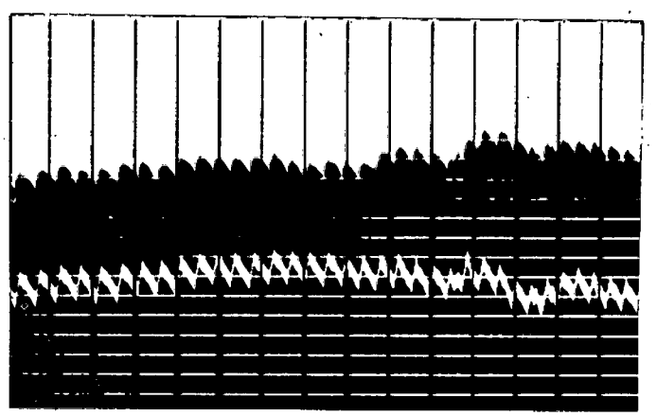


FIGURE 84. - CASE No. 6.

Left middle finger (upper tracing) and right middle finger.

Spontaneous release of spasm.

Number 7.

Mrs M.C., 38, white, female, was first seen on 12/3/46. Her history was of five years' duration. She noticed that her hands were abnormally cold and numb. This was present throughout winter and was more marked on direct exposure to cold. The numbness involved all fingers of both hands. At the same time her hands were also bluish in colour.

A few months after the onset of the condition in the hands, the feet also became involved. The condition was identical both in the hands and feet.

Apart from noticeably cold and blue hands and feet examination was negative.

Plethysmographic records were taken. At rest on 12/3/46 the pulse volume of the right middle finger was 0.003cc. (Figure 85. - page 262). Thermo-regulatory body heating, raised the pulse volume to 0.03cc. (Figure 86. - page 262).

She was diagnosed as having Raynaud's Phenomena and preganglionic section was advised.

On 25/7/46 bilateral lumbar sympathectomy was performed. L.2, L.3 and L.4 ganglia and intervening chain were removed by the extraperitoneal approach on each side.

The right second thoracic ganglion only was removed on 23/8/46. The approach was anteriorly through the second interspace. Through a similar approach on the left side, the sympathetic chain from above the second thoracic ganglion to below the fourth thoracic ganglion, was removed on 19/9/46.

Immediately after operation both hands were warm and dry.

The scars of both wounds tended to undergo keloid formation. X-Ray therapy was given on four occasions. No other complication ensued.

Two months before being re-examined, i.e. in January, 1947, the patient developed cramps in both legs and arms. This appeared in midsummer and occurred at any time of the day or night. This has persisted. There was no relation to cold, emotion, warmth or effort. They were relieved by massage. She experienced numbness in the right hand and right foot. This numbness is vague and indefinite and varying in onset and duration.

Both hands and feet were dry and have been so ever since operation. She had noticed an increased amount of sweating about the body and her face, too, appeared to sweat rather more than formerly.

She returned for re-examination in March, 1947, i.e. six months after sympathectomy of the upper extremities.

Skin temperature readings at rest reveal low records for both hands. After thirty minutes' body heating the temperatures reached 30 - 31°C. On other occasions, however, the skin temperatures of the fingers of both hands have reached 33°C.

The pulse volume of the left middle finger at rest

/was 0.003cc.

was 0.003cc. After thirty minutes' body heating the pulse volume reached 0.02cc. (Figure 87. - page 263).

The pulse volume of the right middle finger at rest was 0.002cc. and after thirty minutes' thermo-regulatory body heating reached 0.02cc. (Figure 88. - page 264).

The effect of a deep breath on the pulse and digital volume of the left middle finger is shown in Figure 89. - (page 265). There is constriction and a fall in the digital volume.

It was noted that after body heating no sweating was present on the hands and forearms. Sweating was also absent on the feet and lower legs but was profuse on the face and body.

Sweating occurred on the hands after pilocarpine injection. It ceased with the administration of atropine. Together with the sweating and fall in temperature, the hands felt cold and were a dusky bluish colour. Plethysmographs show that vasoconstriction occurred following pilocarpine administration. (Figure 90. - page 266).

Conclusions:

Six months after preganglionic sympathectomy the hands of the patient were cold on examination. Both skin temperature and pulse volume recordings had returned to the level existing before sympathectomy.

Although on the right side only the second thoracic ganglion was removed and on the left the chain from the second to the fourth thoracic ganglia inclusive were removed, there was no gross difference on the two sides following sympathectomy.

Vasomotor tone, therefore, has returned as early as six months after sympathectomy.

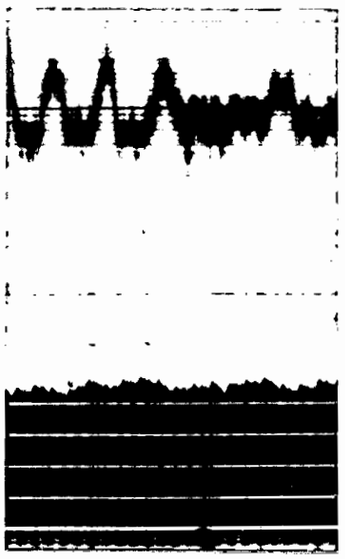


FIGURE 85. - CASE No. 7.

A case of Raynaud's Phenomena.

Right middle finger during an attack before Sympathectomy.

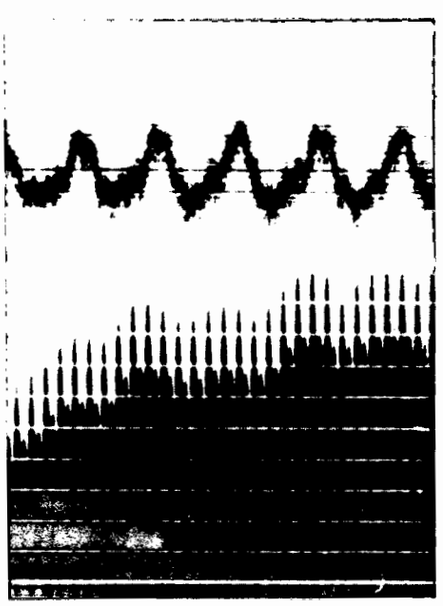


FIGURE 86. - CASE No. 7.

Right middle finger after thermo-regulatory body heating.

Before Sympathectomy.

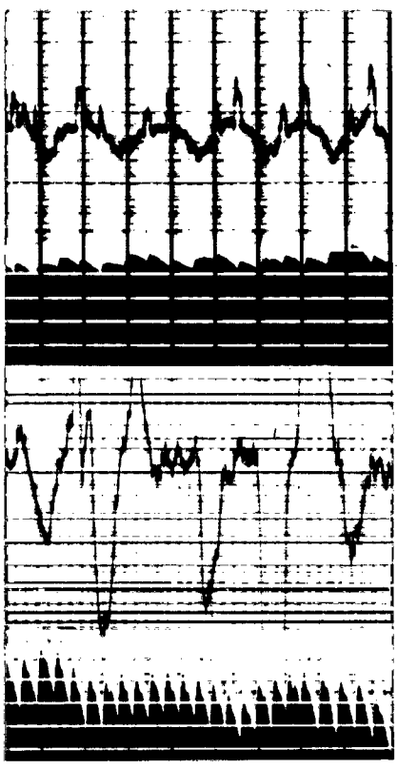


FIGURE 87. - CASE No. 7.

The left middle finger at rest (upper tracing) and after body heating.

Left Th.2, Th.3 and Th.4 removed six months previously.

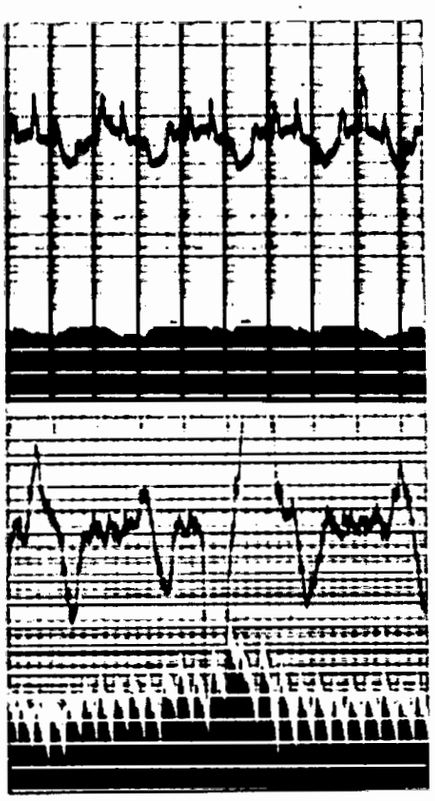


FIGURE 88. - CASE No. 7.

The right middle finger at rest (upper tracing) and after body heating.

Right Th.2 removed six months previously.

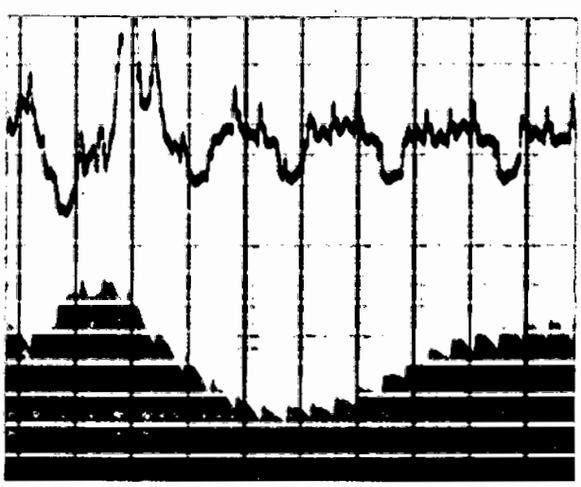


FIGURE 89. - CASE No. 7.

The left middle finger six months after sympathectomy.

Note the effect of a deep breath.

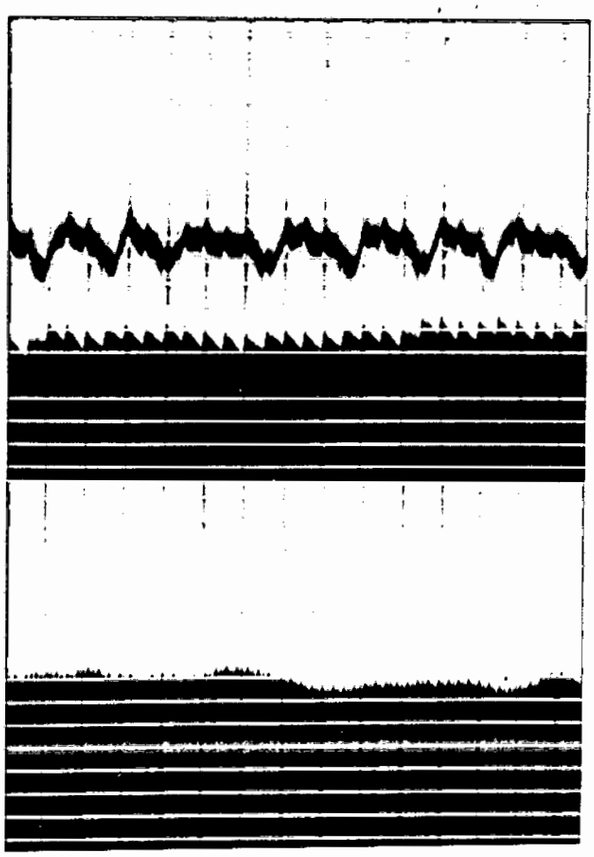


FIGURE 90. - CASE No. 7.

The right middle finger at rest (upper tracing) and after the administration of pilocarpine.

Number 8.

Miss I.B., 42, white, female, was first seen in 1943. Her complaint at that time was "coldness of the hands and feet".

For the previous twenty years her hands were always cold during winter. In addition she experienced attacks of pallor in the hands on exposure to cold, winter or summer. Attacks lasted from five minutes to two hours and could be relieved by plunging the hands into hot water. Pallor was followed by cyanosis and during the stage of pallor numbness was present. As the attack subsided tingling in the fingers was experienced.

Examination was essentially negative. Plethysmography in 1945 revealed a large element of spasm easily relieved by reflex body heating.

Lumbar sympathectomy had been performed in 1943. Since then her feet had been completely relieved.

Thoracic sympathectomy was performed on 7/3/45 and 25/3/45. The second and third thoracic ganglia were cauterised on each side via the thoracoscope. Numerous adhesions had to be divided, before the ganglia were cauterised.

Clincially the hands were warm and dry for a short while post-operatively. A month or two after discharge from hospital, however, attacks of Raynaud's Phenomena appeared again. Some improvement had occurred in that attacks were not as frequent.

Meanwhile the patient has been in and out of hospital for numerous other complaints.

When examined in 1947 both hands were cold. The fingers and distal part of the hand were blue. Attacks of Raynaud's Phenomena could easily be induced by immersion of the hands in cold water.

Plethysmography on 25/11/47 of both hands at rest reveals that the pulse volume is larger on the right than on the left hand, the actual figures being .008cc. and .006cc. (Figure 91. - page 269).

After thirty minutes' body heating the pulse volume of both hands is the same, There has been complete release of vasoconstriction and the vessels are fully dilated at 0.025cc. (Figure 92. - page 269).

The implication, therefore, is obvious that vasomotor tone is present in both hands after cauterisation of the second and third thoracic ganglia three years previously.

Whilst both hands were fully dilated, reflex vasoconstriction was tested by immersing the feet in iced water. Constriction occurred in the left hand but was not so obvious in the right. From this test alone the sympathetic innervation to the left hand is thus intact. On the right hand further proof is necessary that innervation is still complete.

Sweating was observed during the response to reflex body heating. At rest sweating was not apparent on either the face or the hands. After thirty minutes' body heating,

/however,

however, sweating was present on the left hand and left side of the face. No sweating could be observed on the right hand or face.

Confirmatory evidence is, therefore, at hand that the left upper extremity still retains its sympathetic innervation.

The right upper extremity, however, shows conflicting evidence. Whilst vasomotor tone, as judged by body heating, is undoubtedly present, both sweating and reflex response to immersion of the feet in iced water, seem to indicate that the sympathectomy is still partially complete.

In response to pilocarpine gr.1/6 intramuscularly attacks of Raynaud's Phenomena appeared on both hands. Sweating occurred on both sides of the face and on both upper extremities. It was noticed, however, that a small area on the right chest did not sweat.

The pulse volume and digital volume of BOTH hands decreased.

Conclusions:

Investigation of the sympathetic innervation of the upper extremities over two years after cauterisation of the second and third thoracic ganglia, shows that BOTH hands are still under sympathetic control. Return of symptoms occurred within a month or two after sympathectomy.

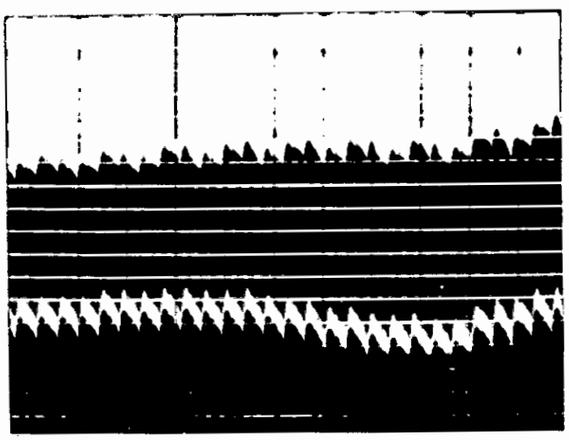


FIGURE 91. - CASE No. 8.

The left middle finger (upper tracing) and right middle finger at rest.

Over two years after cauterisation of Th.2 and Th.3 on both sides.

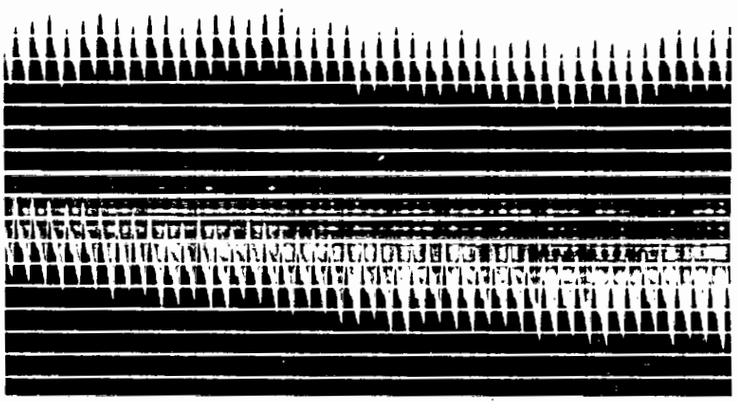


FIGURE 92. - CASE No. 8.

The left middle finger (upper tracing) and right middle finger after thirty minutes' body heating.

Number 9.

Mrs. J.T.R.S., 42, white, female, had had cold feet since childhood. Her feet were always cold during the winter months, especially during the night. No matter how many blankets were applied, the coldness persisted. At the onset of summer and warm weather relief was obtained.

This coldness was associated with a bluish discolouration of the ankles and toes. The blueness was continuous throughout winter and disappeared during the warm weather.

Examination revealed cold extremities with a bluish-purplish discolouration of both legs above the ankles and slight cyanosis of the toes. The dorsum of the foot was normal. There was no trophic disturbance and no oedema.

All the palpable pulses could be felt.

The skin temperatures were only slightly above room temperature in all extremities. In the feet there was a markedly diminished blood flow at rest. But on release of vasoconstrictor tone the skin temperatures reached full vasodilatation level. The pulse volume also increased considerably but only reached 0.012cc. which was somewhat below normal.

Bilateral lumbar sympathectomy was performed in May, 1943 and subsequently her feet have remained warm and dry.

Prior to the lumbar sympathectomy, apart from coldness, her hands were normal.

One month after the operation both hands became cold, during winter. The coldness involved the fingers and hands up to the wrists. The hands and fingers had a bluish-purplish colour.

There was no pain or numbness at this stage. If the hands were warmed, they felt hot and itchy. The hands felt "tight", particularly under the nails. There was never any pallor. Chilblains appeared and her hands became swollen and useless. There was never any excess sweating of the hands.

Examination revealed a similar state of affairs as existed in the feet prior to operation. A marked degree of arterial spasm was present in both hands. This was easily removed by reflex body heating. At full dilatation the pulse volume reached 0.018cc.

Preganglionic sympathetic section was, therefore, undertaken.

On 20/4/46 the right second thoracic ganglion was cauterised via the thoracoscope. The left second thoracic ganglion was similarly cauterised on 6/5/46.

After operation both upper extremities and the face were dry and warm. The post-operative improvement has been maintained. Two months after operation the patient was able to go fishing in mid-winter without any ill effects.

Sweating was completely absent from both hands and the face. She still sweated in the axilla and observed that the amount of sweat present on the body was more than previously.

/Plethysmographic

Plethysmographic examination of the left index finger on 11/6/46, i.e. two months after operation, revealed a resting pulse volume of 0.004cc. (Figure 93. - page 272). After thirty minutes' thermo-regulatory body heating the pulse volume was 0.006cc., as compared with 0.018cc. before sympathectomy. (Figure 94. - page 272).

After reflex body heating on 11/6/47 the pulse volume of the left middle finger was 0.01cc. This is still short of the full-dilatation level reached before sympathectomy.

The right middle finger was tested on 13/6/48. At rest the pulse volume was 0.006cc. (Figure 95. - page 273). After thirty minutes' thermo-regulatory body heating the pulse volume had risen to 0.008cc. (Figure 96. - page 273).

On 9/6/47 the skin temperatures of both hands were recorded whilst at rest. Both hands felt cold but were pink and dry. The temperatures of the left hand were much lower than those of the right. (Figure 97. - page 274). After thirty minutes' thermo-regulatory body heating the temperatures of both hands were equal at 34°C. (Figure 98. - page 274). Both hands felt warm, were a bright pink, and were still dry.

Pilocarpine, intramuscularly, produced vasoconstriction Also sweating was observed on both hands and forearms after pilocarpine. The face also sweated.

Sweating wasabsent on both arms and on the face as judged by the Starch-Iodine test.

Whilst the left middle finger was fully dilated the right hand was immersed in ice water. Although the effect is not as striking as with a non-sympathectomised finger there is a tendency for the digital volume to decrease and the pulse volume shows a definite diminution in amplitude. (Figure 99. - page 275). In the light of this there appears to be some response to reflex cold stimulation. Similar changes were observed on the right side.

This evidence then points to there being some communication between the vessels of both upper extremities and the sympathetic nervous system.

However, other evidence is still strongly in favour of the vessels of the upper extremities still being sympathectomised. There has been no return of symptoms. Sweating is completely absent in response to reflex body heating and also the pulse volume after body heating has not returned to the pre-sympathectomy level.

Conclusions:

It appears, therefore, that the upper extremities are still practically completely sympathectomised over a year after cauterisation of the second thoracic ganglion bilaterally.

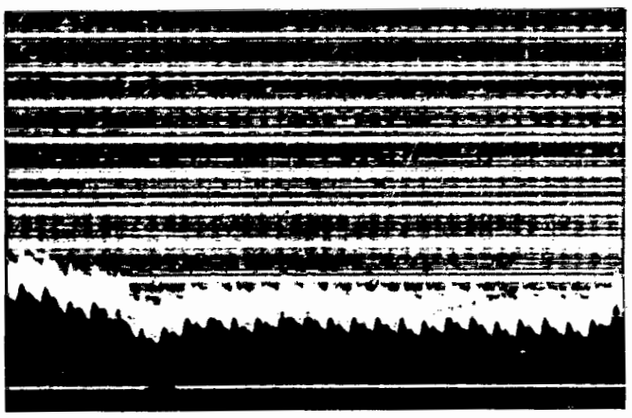


FIGURE 93. - CASE No. 9.

The left index finger at rest.

Two months after cauterisation of the left second thoracic ganglion.

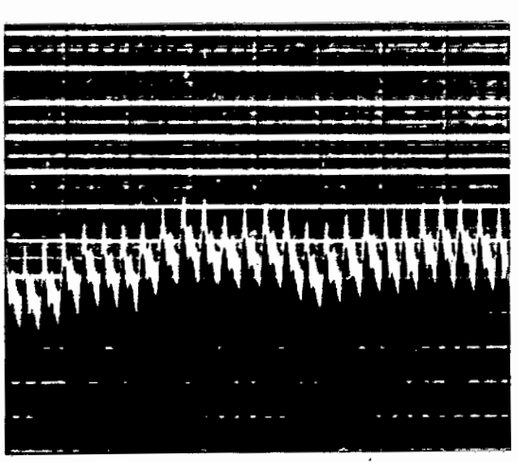


FIGURE 94. - CASE No. 9.

The left index finger after thirty minutes' body heating.

Before sympathectomy.

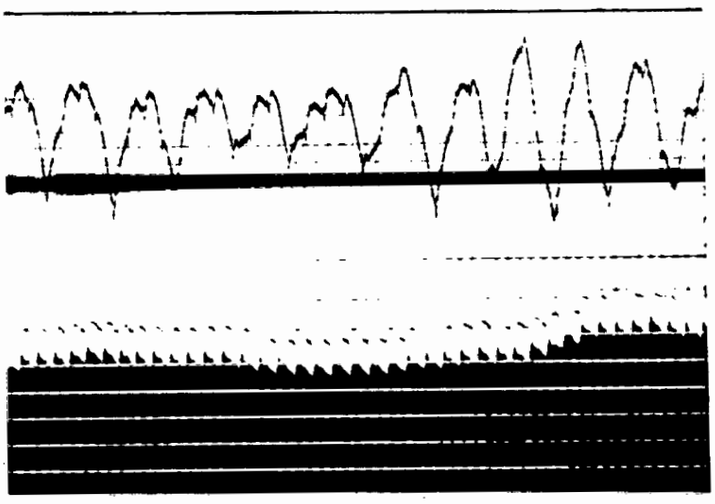


FIGURE 95. - CASE No. 9.

The left middle finger at rest.

Two months after cauterisation of the left second thoracic ganglion.

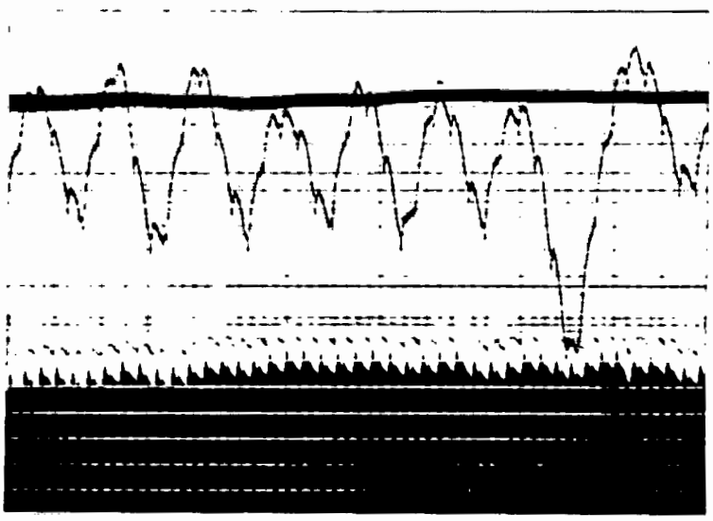


FIGURE 96. - CASE No. 9.

The left middle finger after thirty minutes' body heating.

Two months after cauterisation of the left second thoracic ganglion.

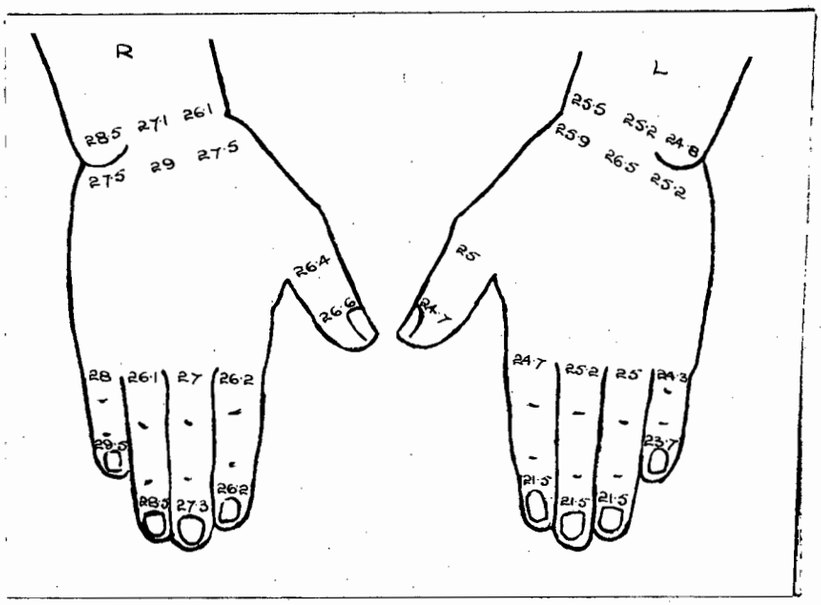


FIGURE 97. - CASE No. 9.

Skin temperatures at rest.

Bilateral cauterisation of the second thoracic ganglia fourteen months previously.

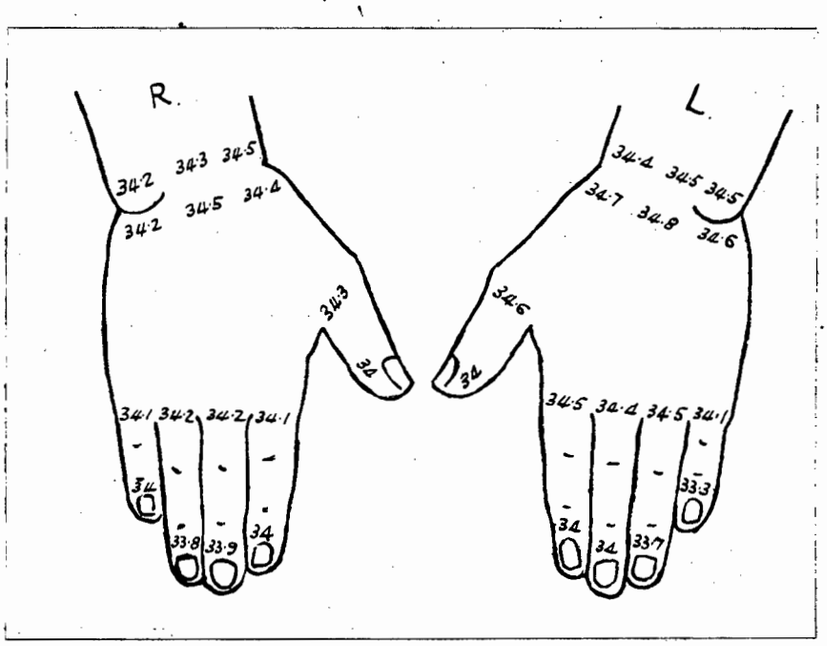


FIGURE 98. - CASE No. 9.

Skin temperatures after thirty minutes' body heating.

Bilateral cauterisation of the second thoracic ganglia fourteen months previously.

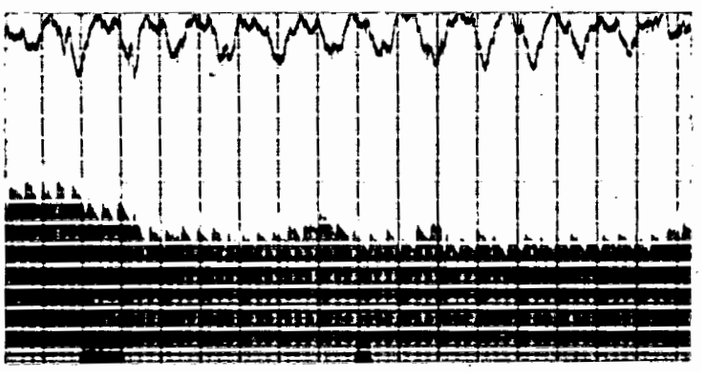


FIGURE 99. - CASE No. 9.

The left middle finger fully dilated.

Immersion of right hand in ice water, during signals.

Cauterisation of left second thoracic ganglion, fourteen months previously.

Number 10.

Mrs B.Ch., 30, white, female, was first seen in 1946. Her complaints were of one year's duration. The left hand was always cold even in warm weather. On exposure to cold the tips of the fingers became white. The pallor lasted for several hours and was succeeded by a bluish-red colour. The attacks were also brought on by emotional disturbances.

The right hand was similarly cold but no pallor or blueness was apparent until shortly before the patient was first seen. However, the attacks were always milder in the right hand and were fleeting in duration.

Both hands became swollen and dusky if exposed to any form of heat.

Examination revealed cold hands but the left hand was perceptibly colder than the right. The pulses on the left side were less easily palpable than on the right. Postural change caused obliteration of the left pulse only.

A fullness in the left supraclavicular region was apparent.

X-Rays revealed a well developed cervical rib on the left side and a rudimentary rib on the right.

The cervical rib was removed on 17/5/46. At the same time the first rib was removed. On leaving the operating table, it was noticed that a left Horner's Syndrome was present. This, however, did not persist and had disappeared in forty-eight hours.

Exploration of the right side failed to reveal either a rudimentary rib or a fibrous band, representing a cervical rib.

However, removal of the cervical rib did not relieve the patient completely. Raynaud's Phenomena, although mild, still occurred in both hands.

On 19/6/46 the sympathetic chain was cauterised through a thoracoscope from above the second thoracic ganglion to below the third ganglion.

The left hand was noted to be warm and dry, subsequent to operation. No further Raynaud's Phenomena have occurred on the left side.

When re-examined eighteen months later, the patient observed that there had been no further attack of Raynaud's Phenomena in the left hand. The right hand still manifested symptoms.

The left hand was slightly warmer than the right. It was dry whereas sweating was present on the right hand. The veins were less prominent on the right hand.

Plethysmography, however, revealed a difference on the two sides. At rest the pulse volume is higher on the left. (Figure 100. - page 278). After reflex body heating

/the pulse

the pulse volume of the normally innervated digit has risen to nearly 0.03cc. The pulse volume of the sympathectomised digit, however, only rose to 0.01cc. (Figure 101. - page 278).

The inability of the sympathectomised digit to dilate in response to reflex body heating is in keeping with the clinical improvement of the patient.

Further measuresto determine the presence or absence of reflex vasomotor tone in the sympathectomised digit were taken. On immersion of both feet in iced water a marked fall occurred in the digital and pulse volumes of the normally innervated right hand. The effect on the sympathectomised left hand was nil. Neither the pulse volume nor the digital volume decreased. (Figure 102. - page 279).

Conclusions:

Sympathectomy of the left upper extremity by cauterisation of the second and third thoracic ganglia is, therefore, still complete eighteen months later.

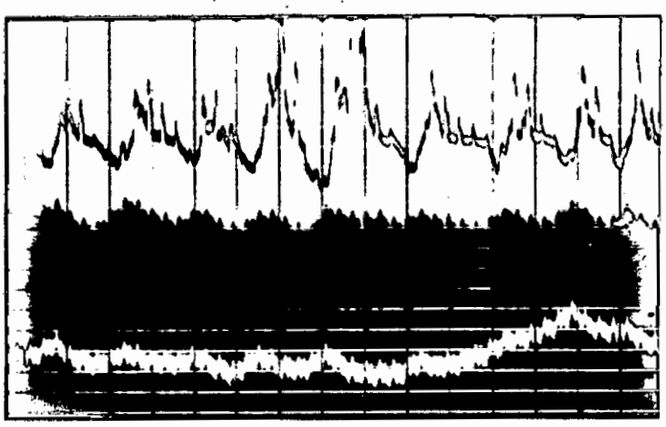


FIGURE 100. - CASE No. 10.

The left middle finger (upper tracing) and the right middle finger at rest.

Left second and third thoracic ganglia removed eighteen months previously.

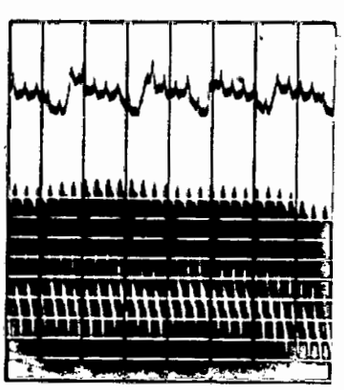


FIGURE 101. - CASE No. 10.

The left middle finger (upper tracing) and the right middle finger after thirty minutes' body heating.

Left second and third thoracic ganglia removed eighteen months previously.

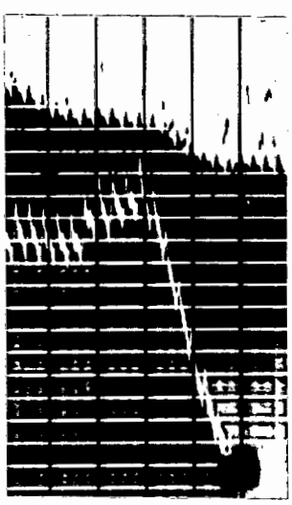


FIGURE 102. - CASE No. 10.

The left middle finger (upper tracing) and the right middle finger.

Left second and third thoracic ganglia removed eighteen months previously.

Both feet immersed in ice water.

Note the effect on the pulse and digital volumes.

Number 11.

Mrs M.B., 57, white, female, was first seen in February, 1946. Eight years previously she had noticed "red patches" on the fingers and neck. These "patches" disappeared in the neck but on the fingers nodules began to form. The nodules increased in size and a patch of whiteness appeared in the centre. Signs of inflammation appeared and the nodules ulcerated and discharged a firm, chalky material. The skin overlying the nodule became thickened.

On several occasions she had "pain" in the hands, which appeared dead-white in colour and felt cold. She was not able to associate this with any known factor. There were no attacks of blueness. The "pain" gradually passed off and the hand became normal in colour.

In addition she had noticed that the skin of the fingers had become thickened. She was unable to use her hands as well as formerly because of the nodules and the thickening of the skin.

There were no other symptoms.

Examination revealed typical calcinosis of the fingers, with scleroderma of the hands.

It was felt that she might be a case of progressive systemic sclerosis, although no changes were demonstrable in the viscera. The evidence of scleroderma was confined to the hands.

Preganglionic sympathectomy of the upper extremities was recommended. At first the patient refused operation but subsequently she consented.

On 29/3/46 the left second thoracic ganglion was cauterised via the thoracoscope. Immediately after operation the left hand was noted to be warm and dry.

On 17/4/46 an attempt was made to cauterise the right second thoracic ganglion via the thoracoscope. Due to a fault in the instrument, however, the attempt had to be abandoned. A subsequent attempt met with the same result. The patient at this stage was still more apprehensive and refused thoracotomy.

Subsequent to operation the patient noticed that her left upper extremity was warm. Although the right hand sweated normally, and even more than normally, the left hand did not sweat at all.

Sweating also was less noticeable on the left side of the face.

There did not appear to be any gross improvement in the calcinosis, although the patient thought there might

/be a diminution

be a diminution in the amount present.

The patient also noticed that when she drank hot liquids or was emotionally upset the right side of the face became flushed; the left side did not.

She had not experienced the "pain" in the left hand and the fingers since operation nor has there been any feeling of numbness.

When examined again fourteen months later there was a difference of 3°C. in the two hands, the left being warmer than the right.

After thermo-regulatory body heating the skin temperature of both hands had reached full dilatation level.

The pulse volumes of the middle fingers of both hands, however, showed a considerable difference after thirty minutes' body heating. The pulse volume on the left was 0.0045cc. whilst that on the right (non-sympathectomised) was 0.015cc.

Sweating in response to thermo-regulatory body heating was completely absent in the left upper extremity and face, whereas on the right sweating was profuse. The right side of the face had a red flushed appearance whereas the left was a pale pink and did not change at all.

The skin resistance of the left upper limb and face was high. The right face and upper extremity registered lower readings except for patches on the thumb and shoulder. The differentiation between the sympathectomised and non-sympathectomised sides corresponds to the areas of sweating.

Pilocarpine produced vasoconstriction in both the normally innervated right extremity and in the sympathectomised left extremity. (Graph 18. - page 195).

Fourteen months after cauterisation of the left second thoracic ganglion the left upper extremity still shows no evidence of return of sympathetic tone. This is borne out by the following features:-

(1) Although there has been little or no improvement in the calcinosis, the attacks of numbness have completely disappeared.

(2) Absence of sweating, noticed by the patient, and confirmed by thermo-regulatory body heating.

(3) The high skin resistance of the left upper extremity and face indicate failure of return of sympathetic function.

(4) The pulse volume does not increase in response to reflex body heating. Although direct heat was not applied in this case the fact that the

/vessels

vessels were capable of further dilatation is noted following the administration of pilocarpine. (Graph 18. - page 195).

Conclusions:

Sympathectomy of the left upper extremity is thus still complete in this patient.

/Number 12.

Number 12.

Mrs du T., 44, white, female, was first seen on 5/11/46 complaining of a severe intractable pain in the left thumb. On 13/7/46 she was pricked in the left thumb by a safety pin. Exploration fourteen days later was performed but no pus found. Thereafter, the pain became very severe.

The pain spread to all the fingers, hand and shoulder. It felt as if the nails were being hammered. Heat did not improve it and cold made it worse. It was not improved by working.

Drugs, X-Ray therapy and diathermy were tried, but no improvement resulted.

In certain positions the hand felt very congested, had a burning sensation and felt as though about to burst.

Examination showed that the left hand was slightly paler than the right. It was slightly mottled and the veins were less prominent than the right. There was no sweating of either palm. A scar was present over the tip of the left thumb.

Hyperaesthesia of the left hand and forearm of the glove type was present.

The skin temperatures were about 1 - 2°C. lower than the right hand.

On body heating the circulation of the left hand reached normal vasodilatation level within the normal time. At full dilatation the skin temperatures were between 33 and 34°C.

The second thoracic ganglion was removed for this causalgia. Relief was marked. The patient was able to use her hand and the pain was relieved. She was conscious only of a prickling sensation in the tip of the thumb which did not interfere with her work.

After operation she noticed that the left hand was not sweating at all. She sweated only on one side of the head and face. The sweating on the normal side appeared to be more than before operation.

Recordings of the skin temperatures four months later revealed that the left hand was about 1 - 2°C. higher than the right hand. After thirty minutes' body heating the right hand reached 34°C. and the left increased to 33°C.

The left hand and arm were dry whereas the palm of the right hand was moist. After thirty minutes' thermo-regulatory body heating sweating was profuse on the right side. The left upper limb and left side of the face did not sweat at all.

/The pulse volume

The pulse volume of the left middle finger at rest was 0.01cc. whereas after thirty minutes' body heating the volume had decreased to 0.009cc. The pulse volume of the right middle finger after thirty minutes' body heating was 0.016cc.

The pulse and digital volume were recorded in response to a deep breath. Whereas no effect was observed in the left middle finger or sympathectomised digit, a marked vasoconstriction occurred in the normally innervated extremity, as judged by a fall in pulse and digital volume.

Although no further tests were performed on this patient, sufficient evidence is present that indicates absence or interruption of the sympathetic supply to the left upper extremity four months after thoracic sympathectomy.

There is absence of sweating both at rest and after reflex body heating. There is no evidence of dilatation of the vessels on reflex body heating. In fact, a slight constriction has occurred. The response to a deep breath, again a reflex mechanism, shows no vasoconstriction, whereas in the normally innervated limb vasoconstriction occurs. Lastly, the causalgia has been cured by sympathectomy.

Conclusions:

Six months after cauterisation of the left second thoracic ganglion sympathectomy, as judged by all tests, is still complete.

/Number 13.

Number 13.

Miss E.S., 22, coloured, female, was first examined on 10/9/46. On that occasion her complaints dated back six months. During those months she had become conscious of blueness of the fingers. This blueness involved all the fingers of both hands and extended over the wrists to the middle of the forearms. The blueness was present throughout the cold preceding winter.

At the same time she found that she was unable to pursue her usual duties as a seamstress. Her fingers felt numb and clumsy. There was no swelling of the fingers. The numbness was particularly marked during the early morning when the coldness of the air was maximal. It improved after use of the hands but was never completely normal.

She was unable to wash in cold water. On immersing her hands, the colour changed to a dead white. This occurred on every occasion on which she washed in cold water. It took some time before the fingers returned to their normal colour.

During the time that her fingers were white she was unable to feel anything with them. When they became warmer, she experienced a feeling of "pins-and-needles".

For the past year she noticed that her feet have been very cold. There have been no associated colour changes.

Examination revealed extremely cold extremities. The skin temperatures were barely above room temperature and the hands from the wrists distally had a bluish tinge. On immersion in cold water a definite pallor of the distal parts of the fingers resulted.

There were no trophic disturbances of the fingers and no evidence of scleroderma.

A diagnosis of Raynaud's Phenomena was made and preganglionic sympathectomy of the upper extremities advised.

Accordingly, on 1/11/46 the right second, third and fourth thoracic ganglia and intervening sympathetic chain were removed by an incision in the third interspace anteriorly. The right hand became warm and dry after operation and was a pale pink colour. Smooth post-operative convalescence was interrupted by a swinging temperature for which no apparent reason was found. 3,200,000 units of penicillin over a period of eight days, however, resulted in complete subsidence of the temperature.

On 5/1/47 it was noted that there was complete relief on the sympathectomised side whereas the left hand was, possibly, colder than before. The right hand was a pale pink colour with no discolouration of the finger tips.

Minor's Starch-Iodine sweating test revealed complete absence of sweating on the right upper limb and

/face.

face. Sweating was profuse on the non-sympathectomised limb and face. (Figure 7. - page 78).

On 15/1/47 the left second, third and fourth thoracic ganglia and intervening sympathetic chain were cauterised with the thoracoscope. No difficulty was encountered and the post-operative course was smooth and uninterrupted.

Immediately after the left sympathectomy the left hand was warm and dry. The colour changed from a dusky blue to a pale pink.

One month later skin temperatures of both hands were recorded whilst at rest. Both hands were warm. The fingers of the left hand were no higher than the right. After thirty minutes' body heating a slight rise only was noticeable. (Figure 103. - page 290).

Plethysmographic records of the left middle finger at this time show the pulse volume to be 0.01cc. After thirty minutes' body heating there was no increase in the height of the pulse volume. (Figure 104. - page 291).

An accidental deep breath is recorded in this figure. At the moment of inspiration there is a barely perceptible rise in the digital volume.

The pulse volume, however, actually shows a slight decrease to 0.0095cc.

The right middle finger sympathectomised two months earlier reveals a pulse volume of 0.009cc. After thirty minutes' body heating no change is observed. (Figure 105. - page 292).

Minor's Starch-Iodine test at this stage revealed complete absence of sweating of both upper extremities. A small amount of sweating was perceptible on the left side of the face. (Figure 9. - page 80).

Posteriorly a well-marked line of demarcation was noted. The line of sweating on the left side extended lower down than the margin on the right. (Figure 8. - page 79).

The whole of the right upper extremity showed a high resistance to the passage of an electrical current. The areas of high resistance extended across the midline, but on the left side the resistance was lower. Patches of high resistance were, however, present. Resistance in the face, which showed slight sweating with the Starch-Iodine test on the left side only, was low on both sides of the face.

On 15/3/47 pilocarpine gr.1/6 was injected intramuscularly. The pulse volume of the right middle finger was recorded continuously. The height of the pulse volume rose from a mean resting level of 0.005cc. to 0.008cc. This increase was maintained for the period that the patient was observed following injection. (Graph 14. - page 191).

The skin temperature of the second finger was recorded at intervals together with that of the left second

/finger.

finger. Whereas the right index finger maintained an even level, that of the left gradually decreased from 30.5°C. to 25.5°C. Clinically the right hand remained warm throughout. The left hand, however, gradually began to feel cold. The colour of both hands was unchanged.

Sweating was present all over the body including the face and hands.

On 29/3/47, i.e. two-and-a-half months after left thoracic sympathectomy, the response of the left middle finger to reflex body heating was noted. The mean resting pulse volume was 0.004cc. After thirty minutes' body heating, by immersion of the right arm in a water bath at 45°C., the pulse volume rose to 0.006cc.

Further, thermo-regulatory body heating produced sweating of the left forehead only. There was no sweating on the upper extremity. Following pilocarpine, however, sweating appeared on the whole of the left face and upper extremity.

On 26/4/47 pilocarpine was once again administered and the effect on the pulse volume of the right middle finger observed. (Graph 15. - page 192).

The pulse volume shows little variation from the mean resting volume of 0.005cc.

The digital volume of the finger, however, reveals what appears to be a decrease before the administration of pilocarpine. The volume then increases until atrophine is given. There is a small decrease, succeeded by an increase - the slope of the curve being practically the same as before atropine.

As on previous occasions the skin temperature of the right index finger showed no gross variation. The left index finger, once again, showed a decrease in skin temperature, not affected by the administration of atropine.

Sweating occurred as on previous occasions.

On 14/6/47, a cold mid-winter day, the skin temperatures of both hands were recorded at rest. (Figure 106. - page 293). The temperatures were lower than at any other time since operation. In spite of this both hands were pink and felt warm. There was no evidence of sweating. It was noticeable that the hair on both forearms had increased in amount since sympathectomy.

After thirty minutes' body heating the temperatures of both hands rose to 32.5°C. No evidence of sweating was observed on either hand. (Figure 107. - page 293).

Skin resistance determinations on the same day showed areas of high resistance (sympathectomised) on both upper extremities. Areas of low resistance were encountered on the left side of the face and on both sides of the forehead.

On 28/6/47 pilocarpine was administered again.

/(Graph 16.

(Graph 16. - page 193). The mean pulse volume of the right middle finger at rest was 0.005cc. A tendency to decrease was present before pilocarpine administration, the lowest reading being 0.0035cc. At the moment of injection the reading was 0.003cc. Immediately after injection of pilocarpine the pulse volume rose to 0.005cc. This was maintained for four minutes and succeeded by a gradual decline in pulse volume. Shortly before the administration of atropine the pulse volume decreased to 0.002cc.

At intervals the pulse volume of the left middle finger was determined. From a resting volume of 0.008cc. there was a decrease to 0.003cc. after pilocarpine, falling to 0.002cc. after atropine.

The skin temperatures of both hands did not show any change from the previous tests.

On this occasion, however, it was noted that, whilst the right index finger felt warm, the right medial three fingers felt cold fifteen minutes after atropine had been administered. The temperatures of these fingers were then taken with the following result:

2 R.F. ... 29.8°C.	2 L.F. ... 24.5°C.
3 R.F. ... 25.8°C.	3 L.F. ... 25.7°C.
4 R.F. ... 23.5°C.	4 L.F. ... 23.5°C.
5 R.F. ... 23.1°C.	5 L.F. ... 23.3°C.

In spite of being cold, the fingers still were pink and dry.

It seemed apparent from the response to thermo-regulatory body heating that both hands were still sympathectomised. This was borne out both by skin resistance and sweating tests. Also a deep breath had no effect on the pulse or digital volume of the right middle finger.

Whereas the pulse volume of the right middle finger did not decrease following pilocarpine and atropine on 26/4/47, vasoconstriction resulted two months later.

The left middle finger, however, on the first occasion tested, four weeks after sympathectomy, constricted in response to pilocarpine.

Sweating was present on the face on the left side in response to thermo-regulatory body heating whereas on the right side it was absent.

It is worthy of note that sympathectomy on the right was carried out by definition and dissection of the sympathetic ganglia and rami. On the left sympathectomy was undertaken by cauterisation. It would be more likely that the left sympathectomy is incomplete.

Conclusions:

Although thermo-regulatory body heating indicates

/that

that vasomotor tone is probably still absent, the vasoconstriction obtained by pilocarpine four weeks after left sympathectomy indicates that operation is probably not complete. Vasoconstriction from pilocarpine only first appeared in the right finger as early as six months after operation.

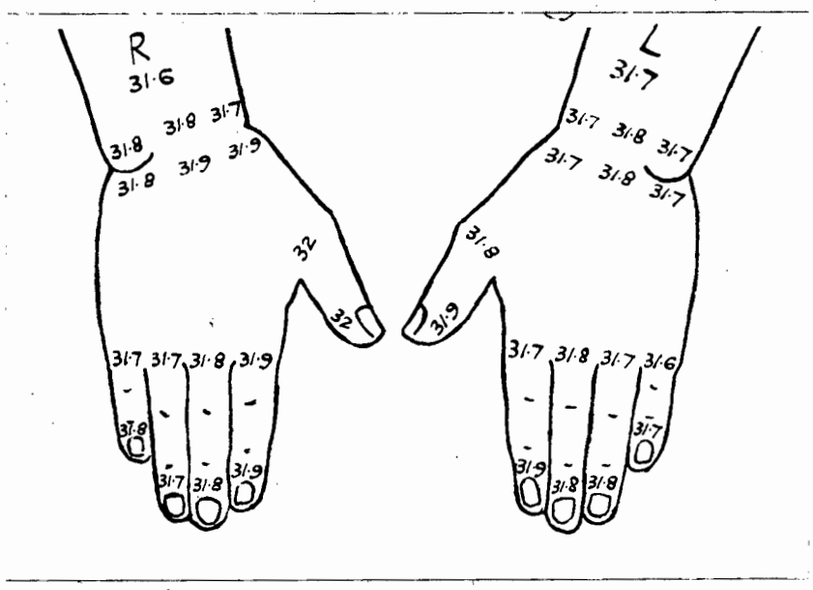


FIGURE 103. - CASE No. 13.

Skin temperatures of both hands
after thirty minutes' body heating.

Three-and-a-half months after removal of the
right Th.2, Th.3 and Th.4 and
one-and-a-half months after cauterisation of
left Th.2, Th.3 and Th.4

Room temperature 26.6°C.

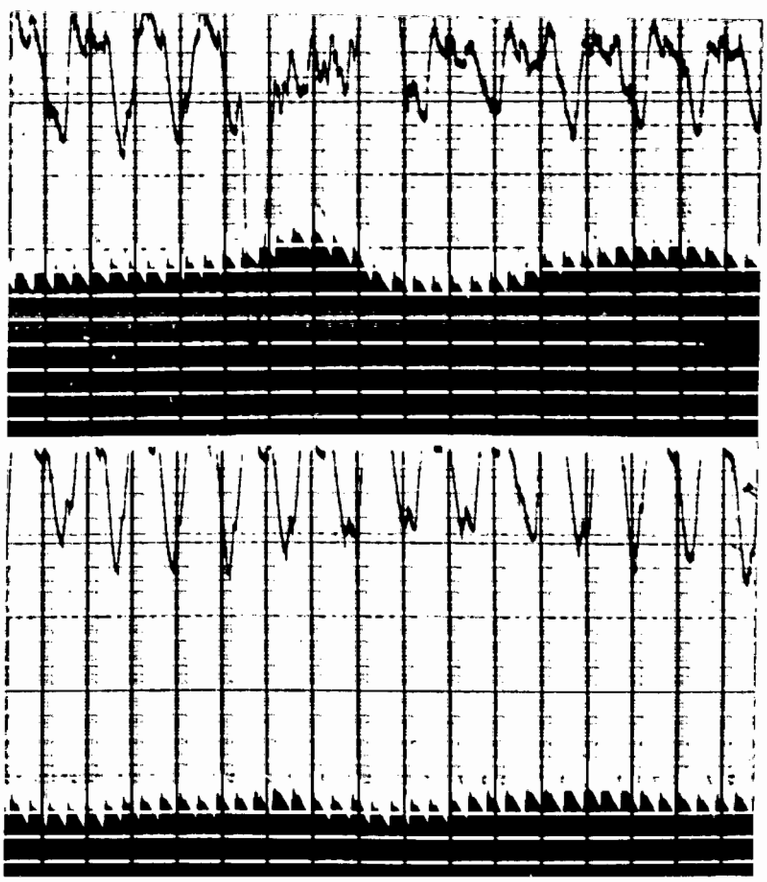


FIGURE 104. - CASE 13.

The left middle finger at rest (upper tracing) and after thirty minutes' body heating.

One-and-a-half months after cauterisation of left Th.2, Th.3 and Th.4.

Note the accidental deep breath recorded in the upper tracing.

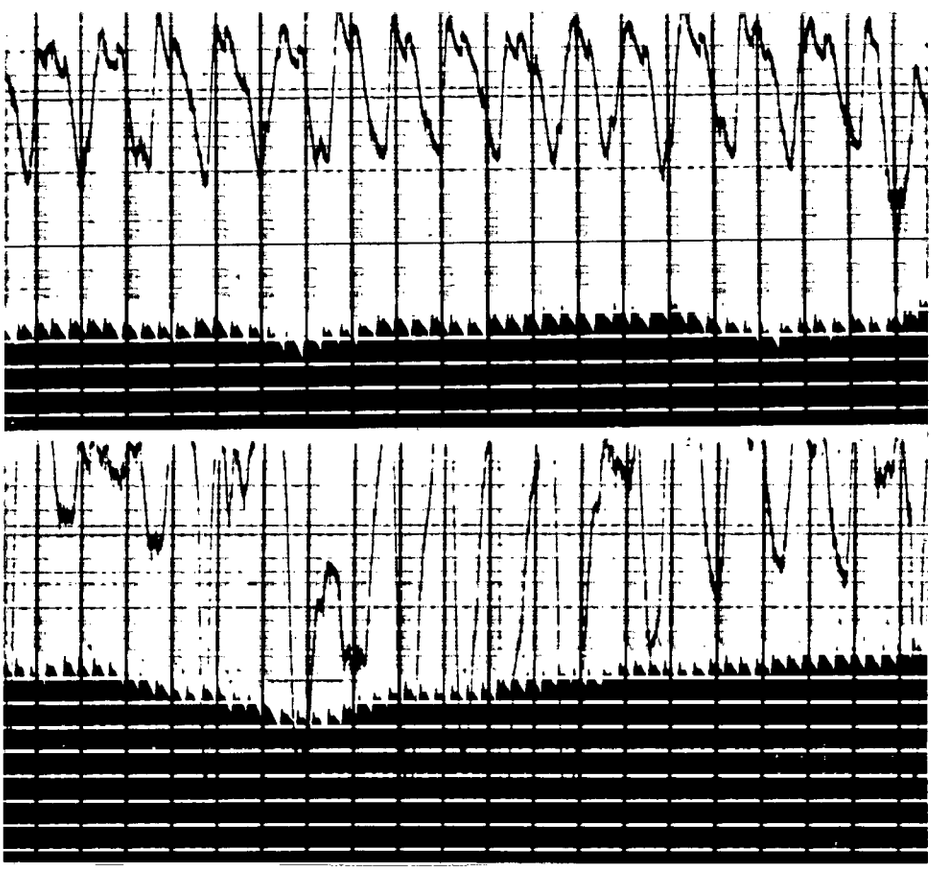


FIGURE 105. - CASE No. 13.

The right middle finger at rest (upper tracing) and after thirty minutes' body heating.

Three-and-a-half months after removal of Th.2, Th.3 and Th.4

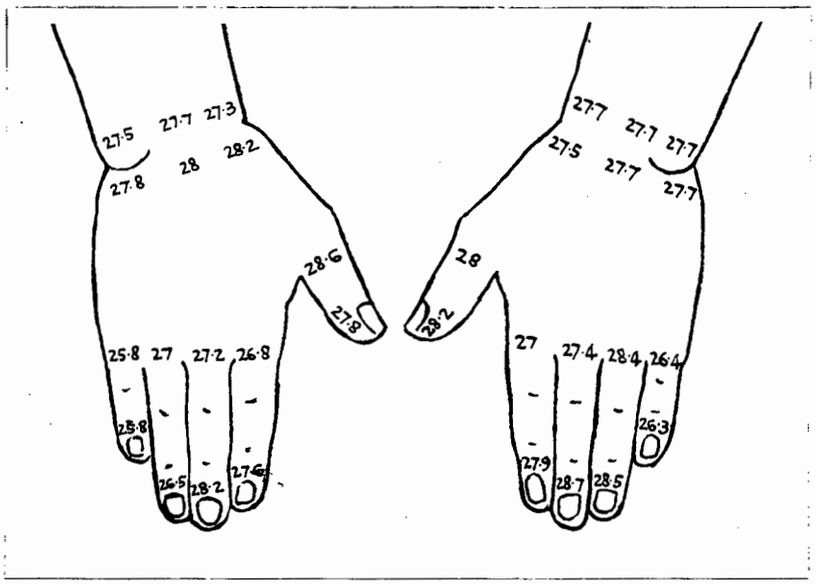


FIGURE 106. - CASE No. 13.

Skin temperatures of both hands at rest.

Seven-and-a-half months after removal of right Th.2, Th.3 and Th.4 and five-and-a-half months after cauterisation of left Th.2, Th.3 and Th.4.

Room temperature 21.7°C.

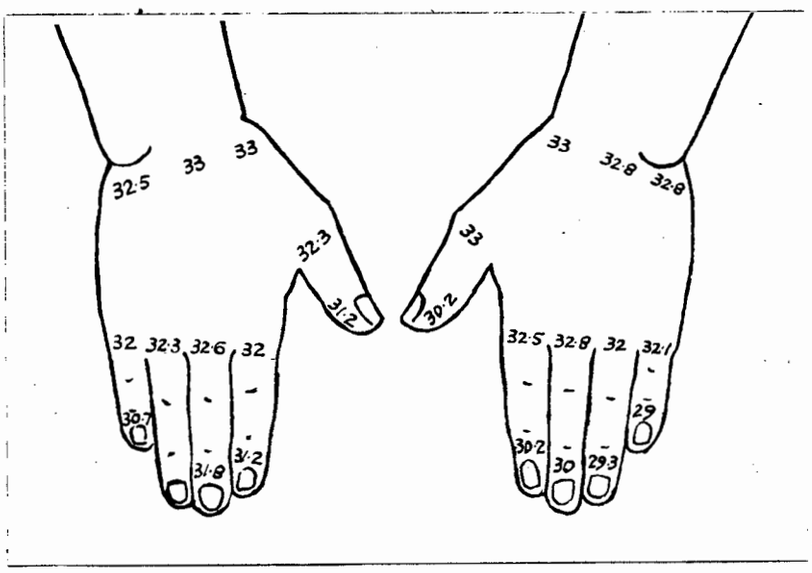


FIGURE 107. - CASE No. 13.

Skin temperatures of both hands after thirty minutes' body heating.

Seven-and-a-half months after removal of right Th.2, Th.3 and Th.4, and five-and-a-half months after cauterisation of left Th.2, Th.3 and Th.4.

Number 14.

Miss L.M.B., 37, white, female, was first seen at Groote Schuur Hospital in 1940. Her complaint at that time was that her fingers were cold and swollen.

For the last twenty years she has had cold fingers during winter. The fingers are cold throughout winter but the coldness is aggravated by immersing her hands in cold water. During the warm summer months her hands are quite normal.

Blueness of the fingers during the winter has been present for twenty years. The blueness is made worse by immersion of the hands into cold water. If the hands are warmed the colour changes to a deep blue-red.

There is no pain or numbness in the fingers or hands normally, even during cold weather. On warming the hands, however, an intense bursting and itching feeling is present.

Throughout the winters of the last twenty years she has suffered severely from chilblains. They occur at the onset of winter and continue until the beginning of summer. They are associated with a severe itching sensation. Ulceration has never occurred.

With the chilblains the fingers of the hand become very swollen and there is gross limitation of use.

The patient had numerous other complaints and had attended every out-patient clinic in the hospital at some time or other.

On 3/7/47 it was observed that both hands were cold and blue. The medial four fingers of both hands were markedly swollen. Numerous chilblains were present on all the digits except the thumbs. All movements at the interphalangeal joints were restricted.

The patient was extremely nervous but general examination revealed nil except a chronic perforation of the left tympanic membrane.

Skin temperature recordings of both hands show very low readings. (Figure 108. - page 298). Plethysmograph records of the middle fingers, showed barely registrable pulse volumes.

After thirty minutes' body heating the skin temperatures had risen to full dilatation level. The plethysmograph showed normal vasodilatation had occurred.

The patient was recommended for sympathectomy of the upper extremities.

On 20/8/47 after an artificial pneumothorax had been induced, the left sympathetic chain was cauterised from the lower border of the third rib to the neck of the first rib via the thoracoscope. The intention was to cauterise the second and third thoracic ganglia and intervening chain.

/Immediately

Immediately after cauterisation, the left hand was noted to be warm. Next day it was observed that a Horner's Syndrome was present on the left side. Thus either a portion of the stellate ganglion had been removed, or the sympathetic supply to the pupil arose at a lower level than usual.

Five days after the left sympathectomy, skin temperature readings of the two hands showed that the left hand was 4 - 5°C. higher than the right. The hand was warm and dry and has remained so since. The right hand in contrast was cold and blue. (Figure 109. - page 298).

Minor's Starch-Iodine sweating test performed on that occasion showed complete absence of sweating on the whole of the left upper extremity, on the left half of the face, and the left half of the chest as far as the base of the breasts. The line of demarcation was in the mid-line. Posteriorly the left half of the neck and the left shoulder, and back as far as the middle of the scapula, did not sweat. (Figure 10. - page 81).

On the eighth post-operative day pilocarpine nitrate gr.1/6 was administered intramuscularly. The mean resting pulse volume of the left middle finger was 0.008cc. At the moment of injection there was no effect on the pulse volume. Within three minutes the pulse volume rose to 0.010cc. This increase was maintained and a maximum of 0.012cc. was attained eleven minutes after injection. A gradual decrease then occurred and the resting level of 0.008cc. was reached thirty-one minutes later and was maintained.

The skin temperature of the left index finger showed a rise of 1°C. for the duration of the test.

In marked contrast to the steady curve of the left middle finger, the pulse volume of the right (non-sympathectomised) middle finger recorded simultaneously varied greatly. The mean resting volume was 0.006cc. but within a few minutes readings of 0.003cc. and 0.009cc. were obtained. Whereas the injection itself had no effect on the pulse volume of the left digit, the pulse volume of the right middle finger dropped sharply from 0.009cc. to 0.006cc. This was succeeded by a rise irregularly maintained at 0.009cc. Twelve minutes after injection a definite decrease in the size of the volume was observed, which continued so that thirty minutes after injection the pulse volume was only 0.002cc. Similarly the skin temperature of the right index finger fell steadily after fifteen minutes.

Sweating occurred all over the body after pilocarpine. There was no apparent difference between sympathectomised and non-sympathectomised areas. (Graph 9. - page 173).

On 4/9/47 the right second, third and fourth thoracic ganglia were removed through the axillary approach. The sympathetic chain was stimulated before removal. Dilatation of the pupil was observed on stimulation of the second thoracic ganglion. It was expected that a Horner's Syndrome would be present on the right after operation.

/After operation

After operation the right hand was warm and dry. On observing the eyes no difference between the two sides was apparent.

Eight days later, however, the fact that there was a left Horner's Syndrome was once again obvious.

Nine days after right thoracic sympathectomy both hands were warm, pink and dry. The skin temperatures at rest were 27 - 28°C. on the left and 29 - 30°C. on the right.

Minor's Starch-Iodine sweating test performed at this time showed complete absence of sweating on both upper extremities. The face was completely free of sweating and the line of demarcation on the chest anteriorly was slightly lower on the left side. Posteriorly, both shoulders were devoid of sweating and here, too, the area of anhidrosis was greater on the right side. (Figure 11., 12. and 13. - pages 82, 83 and 84).

On 23/9/47 the response of the pulse volume to thermo-regulatory body heating was observed. As can be seen on Graph 25. (page 222), there is actually a slight decrease in the height of the pulse volume after thirty minutes' body heating.

There was no apparent rise in digital volume and the skin temperature readings of the index fingers pursued an even course at 31 - 32°C.

On the same day pilocarpine nitrate gr.1/6 was administered intramuscularly. (Graph 13. - page 190). The pulse volume of both middle fingers was recorded, on the plethysmograph simultaneously. The mean resting pulse volume of both middle fingers was 0.01cc. The prick of the needle had no apparent effect but within five minutes of injection a rise in the pulse volume of both sides was noticeable. The rise in pulse volume was greater on the left than on the right. Nine minutes after injection the pulse volume of the right middle finger was 0.016cc. whereas that of the left was 0.022cc. (Figure 110. - page 299). The maximum volumes reached were, on the right 0.018cc. and, on the left 0.026cc.

At the completion of the test forty-five minutes later the pulse volume of the two digits had subsided but was still above the mean resting levels.

The fluctuations in digital volume were plotted and show very little change to be present.

Similarly, skin temperature recordings of both index fingers showed an increase of 1 - 2°C., but no decrease.

Sweating was present on the abdomen and legs but was completely absent on the left side of the face and whole left upper extremity. Sweating was present on the right.

The patient was last observed on 27/10/47. The left Horner's Syndrome was still present and both hands were

/dry and warm

dry and warm. There had been no recurrence of swelling, chilblains or blueness.

There was an increased growth of hair on both forearms as compared with her pre-operative state. The nails, which were previously flecked with white spots, were apparently reforming completely. A well-marked ridge was present at the margin of growth since operation. The newest part of the nail was completely normal.

Conclusions:

There is no apparent difference in the result of cauterisation or removal of the second, third and fourth thoracic ganglia. One month after operation, sympathectomy appears complete on both sides.

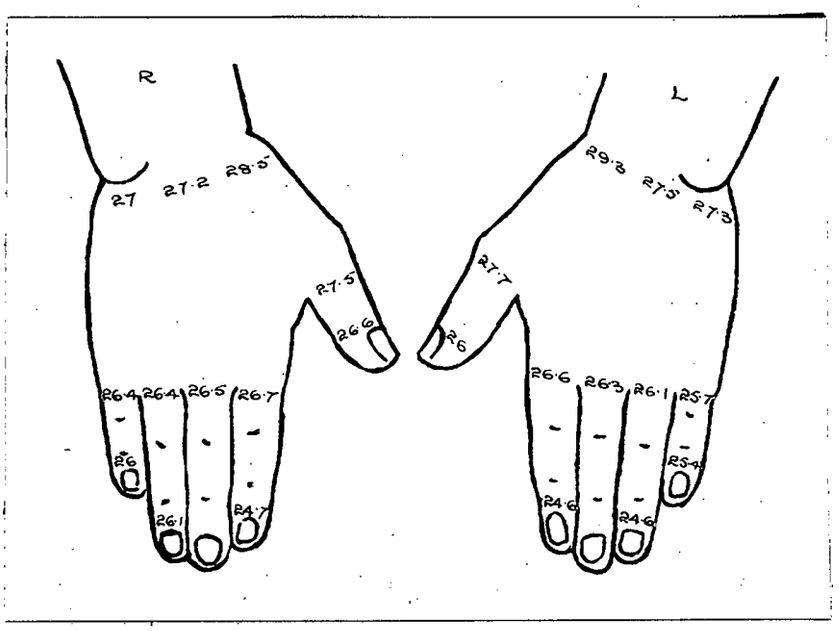


FIGURE 108. - CASE No. 14.

Skin temperatures of both hands at rest.

A case of Raynaud's Phenomena before Sympathectomy.

Room temperature 21°C.

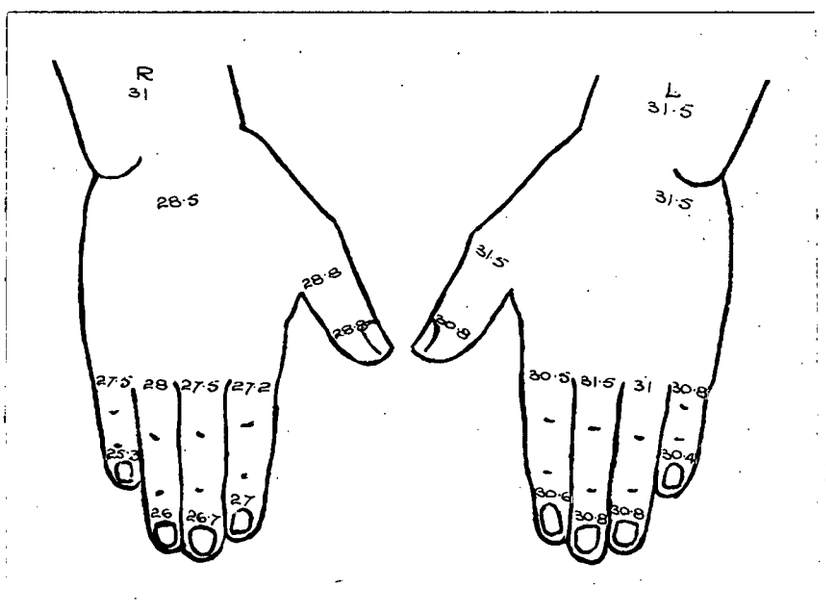


FIGURE 109. - CASE No. 14.

Skin temperatures of both hands at rest.

Five days after cauterisation of left Th.2, Th.3 and Th.4

Room temperature 23°C.

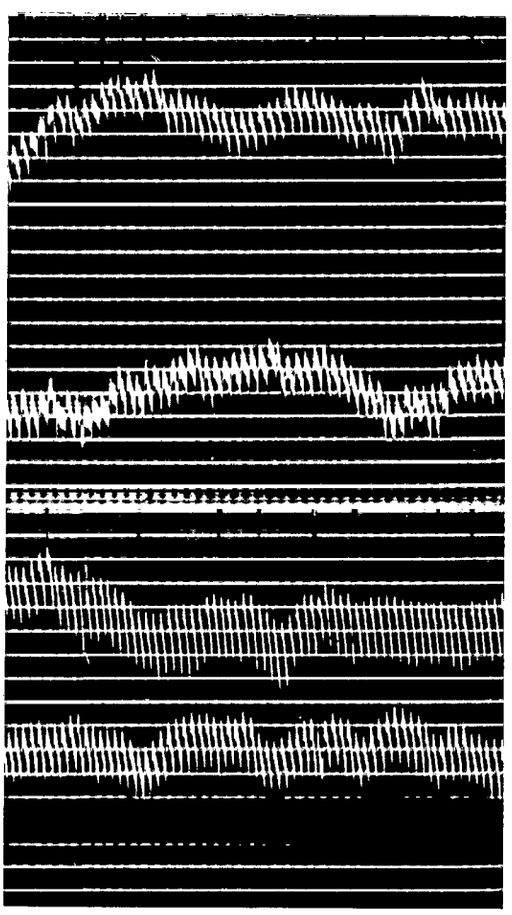


FIGURE 110. - CASE No. 14.

The left middle finger and right middle finger at rest (upper tracing) and nine minutes after pilocarpine gr.1/6.

One month after cauterisation of left Th.2, Th.3 and Th.4 and nineteen days after removal of right Th.2, Th.3 and Th.4.

Number 15.

Miss J.E., 22, white, female, was first seen on 7/5/47. The hands and feet had been cold during winter for the previous five years. It seemed as if the coldness had been getting progressively worse with each succeeding winter. During the warm summer months her hands were normal except when exposed to cold water or a cold wind. The coldness was relieved by use of the hands but was not relieved by the wearing of warm woollen gloves. The right hand was colder than the left.

The hands were always a bluish colour. There was never any whiteness even when inserting the hands in ice water. The blueness persisted throughout winter. If the hands were warmed they became a deep red.

Numbness of the hands was present but never any pain. The numbness occurred on exposure to the more severe degrees of cold. It improved with the use of the hands. On warming the hands the numbness was succeeded by a burning feeling.

There was never swelling of the hands and the patient has not suffered from chilblains.

The feet were involved in an identical way to the hands.

On examination, the patient had cold and blue hands and feet. No trophic changes were present. All the peripheral pulses were palpable.

Skin temperatures of both hands at rest were just above room temperature. (Figure 111. - page 305). After thirty minutes' thermo-regulatory body heating the skin temperatures of both hands rose to full dilatation level. (Figure 112. - page 305).

The mean resting pulse volume of the right middle finger was 0.004cc. At full dilatation the pulse volume was 0.039cc. (Figure 113. - page 306).

Thus a marked spastic element was present, which was completely relieved by reflex heating. Bilateral thoracic sympathectomy was thus advised.

Prior to sympathectomy pilocarpine gr.1/6 was administered intramuscularly. On this occasion both hands were blue and cold. There was no evidence of sweating at the outset of the test. The mean resting pulse volume was 0.005cc., but shortly before the injection, the pulse volume of the right middle finger unaccountably rose to 0.012cc. Pilocarpine was given at this moment of dilatation and, with the prick of the needle, the pulse volume decreased to 0.006cc. A further decline gradually occurred to 0.002cc. one hour after injection. At no stage had any dilatation occurred after pilocarpine.

The digital volume of the finger had shown a tendency to rise before the administration of pilocarpine. Apart,

/from one peak

from one peak five minutes after injection, a progressive decrease occurred, reaching a basal level forty minutes later.

The skin temperature of the right index finger increased from 18°C. to 21°C. before injection. The following reading, two minutes after pilocarpine, was 23.3°C., while three minutes later it was 23.8°C. Thereafter there was a gradual fall to 20.4°C., sixty-eight minutes after injection. The left index finger showed a similar gradient, although the initial rise was not as marked as on the right side and the decline was less obvious.

Sweating occurred all over the body in response to pilocarpine.

On 23/5/47 the right thoracic cavity was entered after preliminary artificial pneumothorax had been induced. The approach was anteriorly via an incision in the third intercostal space. The cartilages of the third and fourth ribs were divided and a rib-spreader employed to enlarge the aperture.

The sympathetic chain was easily identified and the overlying pleura divided and separated. By blunt dissection the chain was exposed from the stellate to below the fourth rib.

The fingers of the hand had been connected to plethysmograph tubes which, in turn, were attached to a mounted pipette. Electrical stimulation, of the chain was then performed and the effect on the pupil and pulse and digital volume noted.

On application of the stimulator to the stellate ganglion, an increase in heart rate was at once apparent; vasoconstriction of the digits occurred and a dilatation of the pupil resulted. On stimulation of the second thoracic ganglion the same changes occurred, but stimulation of the third thoracic ganglion, however, only resulted in a fall in digital volume. No effect was observed either on the heart rate or on the pupil.

It was decided to remove the second, third and fourth thoracic ganglia.

Following the removal of this portion of the sympathetic, the intervening bed and the cut caudal end was stimulated in an attempt to decide whether any fibres had been left unsectioned. Stimulation of the distal stump, second and third intercostal nerves and the bed of the sympathetic over the second and third ribs was without effect on the heart, pupil or pulse.

Stimulation of the stellate ganglion at this stage still resulted in an increase in pulse rate, dilatation of the pupil and diminution in the pulse and digital volume.

The post-operative course was uninterrupted.

Before the patient was moved from the theatre, the right limb was warmer than the left. No change was, however, observed in the pupil at this stage.

/Twenty-four hours

Twenty-four hours later the right upper limb was warm and dry. The right pupil was slightly smaller than the left and there was a slight but definite ptosis. Thus, there resulted, not unexpectedly, a Horner's Syndrome.

The Horner's Syndrome persisted until the eighth post-operative day when it was observed to be absent. It appears likely that the main sympathetic outflow to the pupil was from the first thoracic ramus, but in this case, some fibres arose from the second thoracic ganglion.

Five days after operation skin temperatures of both hands at rest show the fingers of the sympathectomised limb to be 10°C. higher than the normally innervated limb. (Figure 114. - page 307).

The mean resting pulse volume of the right middle finger was 0.03cc. (The fully dilated value was 0.039cc.) After thirty minutes' body heating it was 0.026cc. - an actual decrease being present.

Sweating in response to thermo-regulatory body heating occurred on the left upper limb and left half of the face only. There was no evidence of sweating on the right half of the face and right upper extremity at all.

On the sixth post-operative day pilocarpine gr.1/6 was administered intramuscularly. (Graph 11. - page 188). The mean resting pulse volume of the right middle finger was 0.018cc. (Figure 115. -page 307). Within two minutes of injection the pulse volume had risen to 0.03cc. The maximum height reached was 0.035cc. (Figure 116. - page 308). This level was maintained for six minutes but thirteen minutes after injection the pulse volume had fallen to 0.026cc. At the fourteenth minute atropine 0.5mgm. was administered intravenously. An almost immediate (within fifteen seconds) fall to 0.014cc. occurred, simultaneous with an increase in pulse rate to 144. On continuing the recording the pulse volume gradually returned to the mean resting pulse volume of 0.018cc.

Although a tendency to rise was noted in the digital volume before pilocarpine, the curve was much steeper after injection. A momentary decrease in digital volume occurred at the moment of injection. Similarly, after atropine injection, a slight fall occurred but was succeeded by a progressive increase, reaching a peak thirty-eight minutes later.

Throughout the test the skin temperature of the sympathectomised right index finger did not vary, remaining at 32 - 33°C.

The normally innervated left index finger, however, showed some fluctuation in skin temperature. There was a slight rise from 22.8°C. to 24.3°C. before pilocarpine. Following pilocarpine the temperature had declined to 23.5°C. The decline continued after atropine reaching 22°C. twenty minutes later. Fifty-five minutes after atropine the temperature of the left index finger had risen to 25.8°C.

Sweating occurred on both sympathectomised and normally innervated areas and no distinction could be drawn between the two, as judged by sweating after pilocarpine.

/On 4/7/47

On 4/7/47 the left second, third and fourth thoracic ganglia were removed. The approach on this side was identical to the right. Stimulation was attempted before removal, but, owing to a fault in the connections, no result occurred on stimulation.

Immediately after operation the left hand was warm and dry. There was no Horner's Syndrome on this side.

The skin temperature of the left hand was 1°C. higher than the right.

On the eighth post-operative day pilocarpine gr.1/6 was administered intramuscularly. (Graph 12. - page 189). The mean resting pulse volume of the left middle finger was 0.015cc. whilst that of the right middle finger was 0.0088cc. Within five minutes of injection there was a rise of pulse volume of the left middle finger to 0.022cc. The volume of the right middle finger at the same point was 0.012cc. The increase in the volume of both fingers was maintained for four minutes. Atropine was given by intramuscular injection eighteen minutes after pilocarpine. The pulse volume was maintained at a level of 0.017cc. for eight minutes followed by a decrease to 0.013cc., coincidental with an increase of pulse rate to 95.

At this point the volume of the right middle finger was 0.006cc. at which level it remained until the end of the test.

The skin temperatures of both index fingers did not vary throughout the test, the temperature of the left finger being 1 - 1.5°C. higher than the right.

Sweating occurred all over the body in response to pilocarpine and no distinction could be drawn between sympathectomised and normally innervated skin by this method.

On 18/10/47, well over three months after the latter operation, the patient was seen again. She had no further complaints about the hands, both being warm and not sweating. She considered the result to be excellent.

Minor's Starch-Iodine sweating test was performed. Sweating was absent on the whole of both upper extremities. A slight amount was present on the left forehead but nothing on the right side of the face. (Figure 5. and 6. - pages 76 and 77).

NOTE:

The mean resting pulse rate after sympathectomy was 50 - 60. (Figure 117. - page 308). Immediately after pilocarpine had been injected intramuscularly there was a gradual increase in rate to 84, reached in seven minutes. For the next ten minutes the average rate was 70 - 78. Immediately after the injection of atropine a decrease in rate occurred

/to 54 which,

to 54 which, after three minutes, fell to 48 beats per minute, (Figure 118. - page 309). The heart continued beating at this rate for a further five minutes, after which a steady but rapid rise took place to 90 - 96 beats per minute.

The resting pulse rate of this patient can be considered to be slightly slower than normal, i.e. after sympathectomy. It is of interest that, on stimulation of the sympathetic ganglia at operation, an increase in cardiac rate was noted when the stellate and second and third thoracic ganglia were stimulated. Stimulation of the fourth ganglion was without effect.

It is thus likely that, on removal of the second to fourth ganglia, the synapses concerned with the sympathetic supply to the heart were interruped. This applies certainly to the direct cardiac fibres. As it was uncertain what the sympathetic supply form the left side was, due to failure of the stimulator to function, it is not unlikely that the same ganglia supply the heart on the left side. This would mean complete sympathetic denervation of the heart. It also implies that the reactions of the heart are to the drugs themselves and not via the sympathetic nerves.

It is also worthy of note that the slowing of the heart had not occurred when only a right sympathectomy had been done.

From the foregoing it appears that the initial action of pilocarpine on the heart was increase of rate, but as more of the drug was being absorbed, the effect became that of the vagus, with marked slowing. It is likely that the decrease in rate immediately after the injection of atropine is purely coincidental.

Atropine was injected intramuscularly on this occasion and its effect thus only became manifest after some time. Sweating and salivation ceased only eleven minutes after atropine administration and, as this time corresponds with the increase in heart rate after the slowing, it is reasonable to assume that the slowing of the heart rate cannot be attributed to the injection of atropine, but rather to the vagus-like effect of pilocarpine.

Thus, it is possible that by bilateral removal of the second, third and fourth thoracic ganglia the sympathetic supply to the heart may have been completely extirpated.

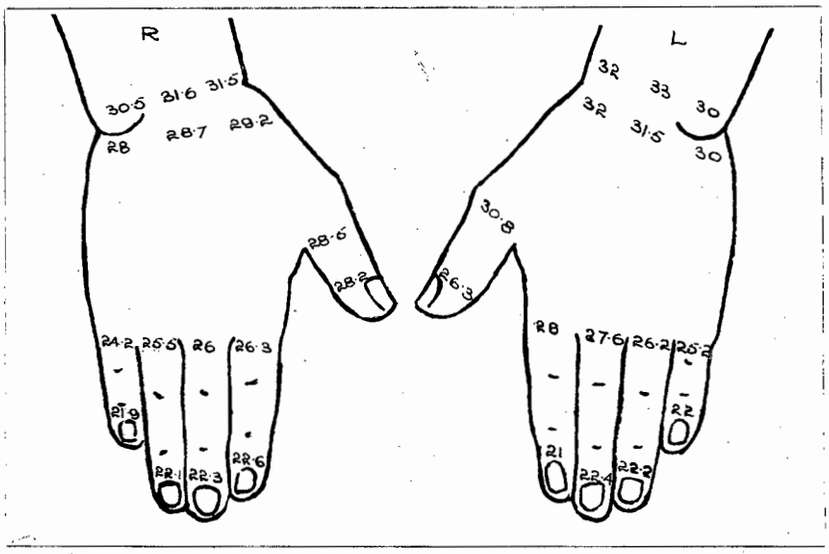


FIGURE 111. - CASE No. 15.

Skin temperatures of both hands at rest.

A case of Raynaud's Phenomena before Sympathectomy.

Room temperature 19°C.

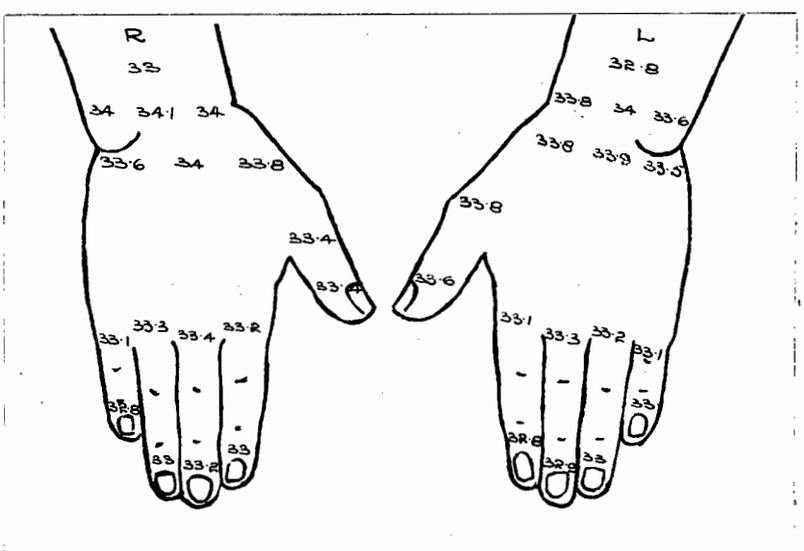


FIGURE 112. - CASE No. 15.

Skin temperatures of both hands
after thirty minutes' body heating.

A case of Raynaud's Phenomena before Sympathectomy.

Room temperature 19°C.

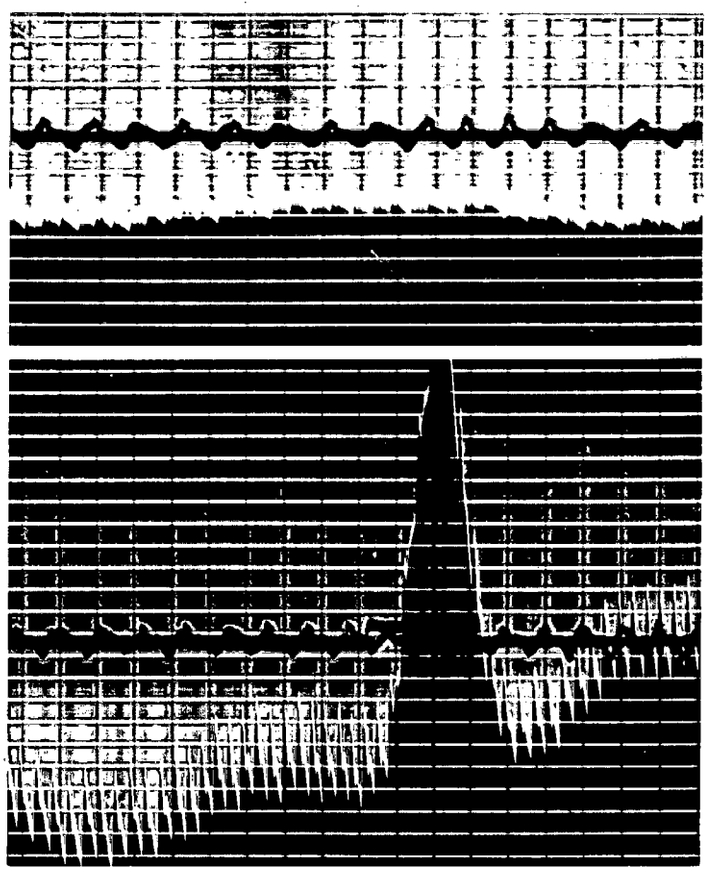


FIGURE 113 - CASE No. 15.

The right middle finger at rest (upper tracing) and after thirty minutes' body heating.

A case of Raynaud's Phenomena before Sympathectomy.

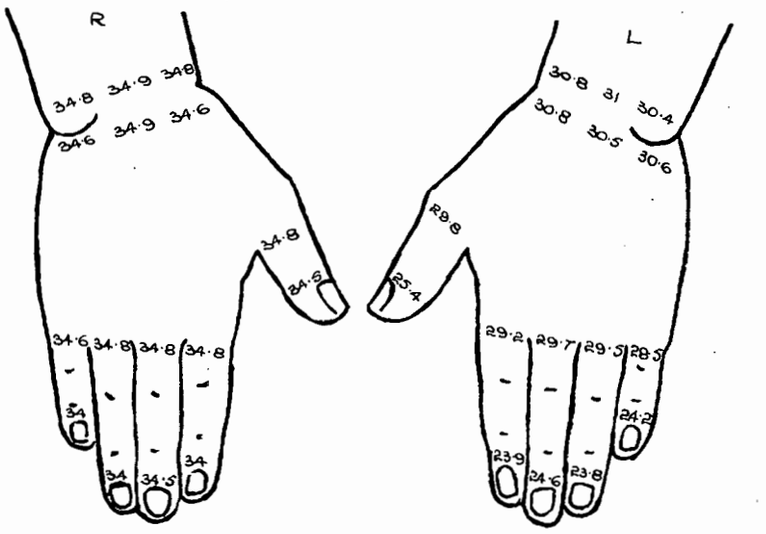


FIGURE 114. - CASE No. 15.

Skin temperatures of both hands at rest.

Five days after removal of right Th.2, Th.3 and Th.4.

Room temperature 19.4°C.

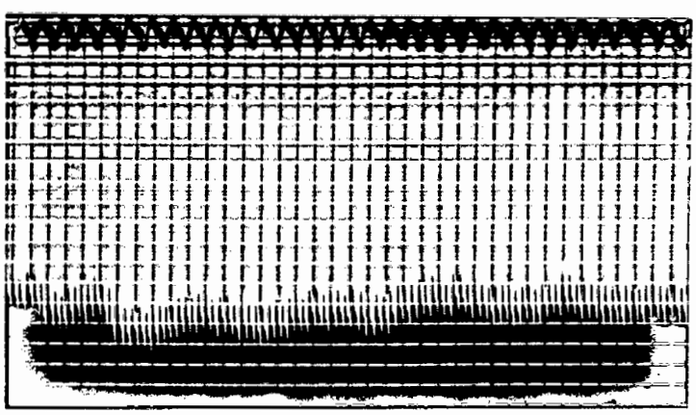


FIGURE 115. - CASE No. 15.

The right middle finger at rest.

Six days after removal of right Th.2, Th.3 and Th.4.

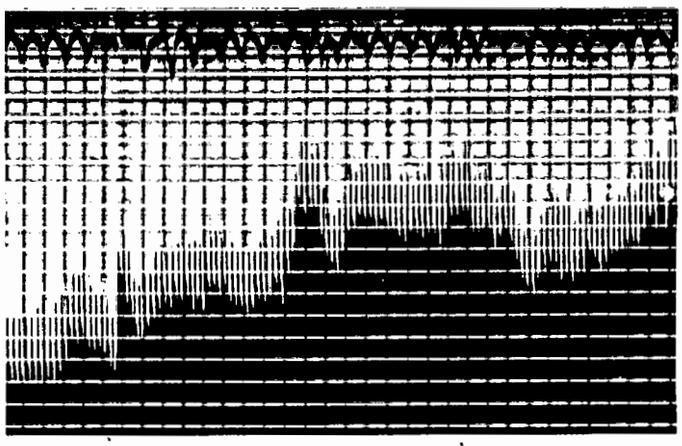


FIGURE 116. - CASE No. 15.

The right middle finger ten minutes after pilocarpine.

Right Th.2, Th.3 and Th.4 removed six days previously.

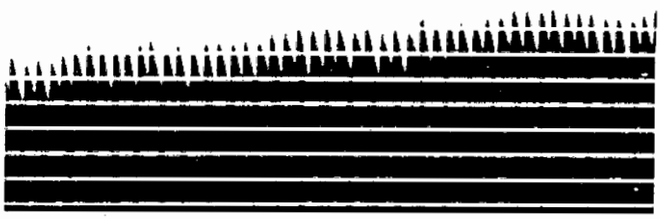


FIGURE 117. - CASE No. 15.

The left middle finger at rest.

Eight days after removal of the left Th.2, Th.3 and Th.4.

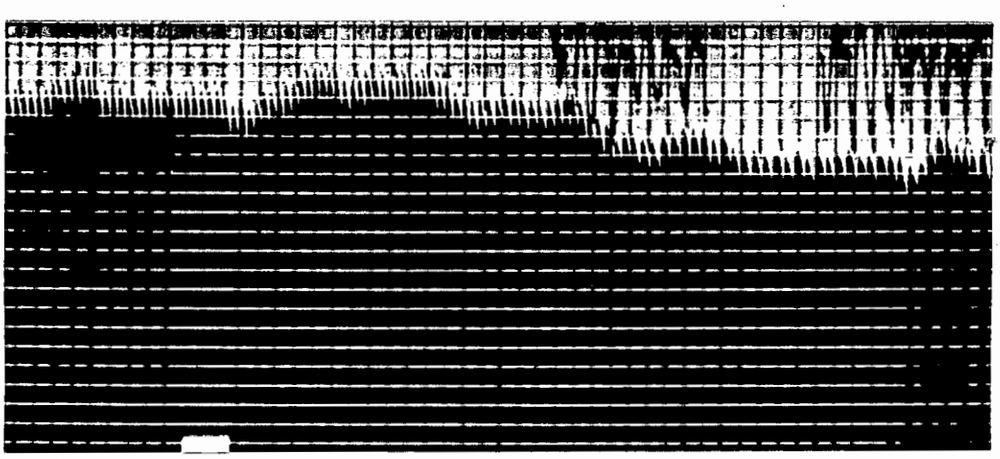


FIGURE 118. - CASE No. 15.

The left middle finger
eighteen minutes after pilocarpine.

Left Th.2, Th.3 and Th.4 cauterised eight days previously.

At signal 0.5mgm. atropine given intramuscularly.

Note the pulse rate.

Number 16.

Miss I.M., 23, white, female, was perfectly well until one year previously. She then noticed that her fingers became numb during the cold weather. At the same time they were white in colour. This was succeeded by a bluish colour and, on putting the hands into warm water, they became painful and very red. The attacks of pallor and blueness lasted for an hour or two and then passed off. The hands felt cold and were clammy.

The attacks were present whenever she exposed her hands to cold and occurred during the summer months too. Anger or other emotional disturbance did not result in an attack.

She had also noticed that her feet were cold throughout winter. When she rose in the morning her toes were white and numb. If she warmed them, they, too, became red and painful. The feet had been involved for about a year.

There were no other complaints.

Examination at room temperature revealed cold, clammy extremities. The tips of the fingers were white and the hands bluish in colour. No trophic changes were seen. Skin temperature readings of both hands were just above room temperature. (Figure 119. - page 312). The pulse volumes of both hands were barely registrable on the plethysmograph.

After thirty minutes' thermo-regulatory body heating, however, a marked change occurred. The skin temperatures of both hands rose to full dilation level. (Figure 120. - page 312). The pulse volumes, too, rose to approximately 0.04cc. on either hand.

With a diagnosis of Raynaud's Phenomena sympathectomy was advised and performed.

On 11/9/47 the left thoracic cavity was entered via the axilla. Many adhesions were present at the apex. These were divided and the sympathetic chain exposed. The second, third and fourth thoracic ganglia, together with the intervening trunk, were removed. On leaving the table the left hand was warmer than the right.

No Horner's Syndrome was present at any period postoperatively.

Eight days later skin temperatures of both hands were recorded. (Figure 121. - page 313). The left hand was 5 - 7°C. higher than the right. It was impossible to estimate the pulse volume of the right middle finger at rest. The pulse volume of the resting left middle finger, however, was 0.01cc.

On the eleventh post-operative day a continuous plethysmographic record was made of both middle fingers simultaneously. Graph 24. (page 207) depicts the changes occurring during thirty minutes' thermo-regulatory body heating.

The pulse volume of the left (sympathectomised) digit

/had a mean

had a mean resting level of 0.01cc. After thirty minutes' body heating the pulse volume was 0.009cc. A slight decrease had actually occurred.

In marked contradistinction, the mean resting pulse volume of the normally innervated right middle finger was 0.001cc. After thirty minutes' body heating the pulse volume was 0.034cc.

Whilst a rise of 0.5cc. occurred in the digital volume of the left middle finger, the digital volume of the right middle finger increased by 1.8cc.

The skin temperature of the left index finger varied slightly between 30°C. and 31.5°C. The skin temperature of the right index finger rose from a resting 22.4°C. to 33°C. at full dilatation.

Minor's Starch-Iodine sweating test, performed on this occasion, showed complete absence of sweating on the left upper extremity. Absence of sweating was also complete on the left half of the face. The line of anhidrosis extended to the midline. (Figures 3. and 4. - pages 74 and 75).

Skin resistance estimation confirmed the extent of sympathectomy. Except for an area of low resistance on the left cheek and lower jaw, the whole of the left upper extremity had a high resistance, indicating absence of sympathetic connections. (Figures 38. and 39. - pages 131 and 132).

Pilocarpine nitrate gr.1/6 was administered intramuscularly on the twelfth post-operative day. (Graph 8. - page 172). At the outset the mean pulse volume of the sympathectomised left middle finger was 0.008cc. Within five minutes of injection a rise in volume was discernible. The pulse volume rose to 0.015cc. and was maintained at this level for a further ten minutes. The rise was followed by a gradual decline to the previous resting level. The digital volume increased by 0.4cc.

The pulse volume of the normally innervated right middle finger fluctuated between 0.02cc. and 0.035cc. The digit was apparently fully dilated. At the moment of injection the pulse volume dropped from 0.03cc. to 0.025cc. This was succeeded by an immediate dilatation to 0.04cc. which, with many fluctuations, reached 0.048cc. fourteen minutes after injection. A sharp decline in pulse volume then occurred till, at the termination of the test fifty minutes after injection, the pulse volume was 0.002cc.

A fall of 1.6cc. in the volume of the right middle finger occurred after injection.

The sympathectomised hand remained warm throughout the duration of the test, whereas the right hand felt cold forty minutes after injection. The temperatures of both index fingers were plotted and showed that the left finger varied between 30°C. and 31°C. The right finger was at the full dilatation level - 33°C. - at the onset. A slight rise occurred after injection, but was succeeded by a rapid fall to 26.5°C. at the conclusion of the test.

Apart from the left axilla, which remained dry throughout the test, sweating occurred on all parts of the body.

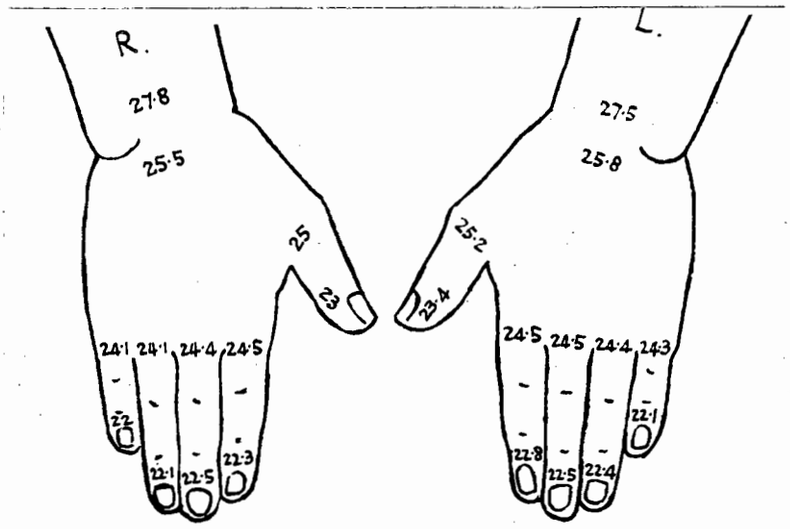


FIGURE 119 - CASE No. 16.

Skin temperature of both hands at rest.

A case of Raynaud's Phenomena before Sympathectomy.

Room temperature 21°C.

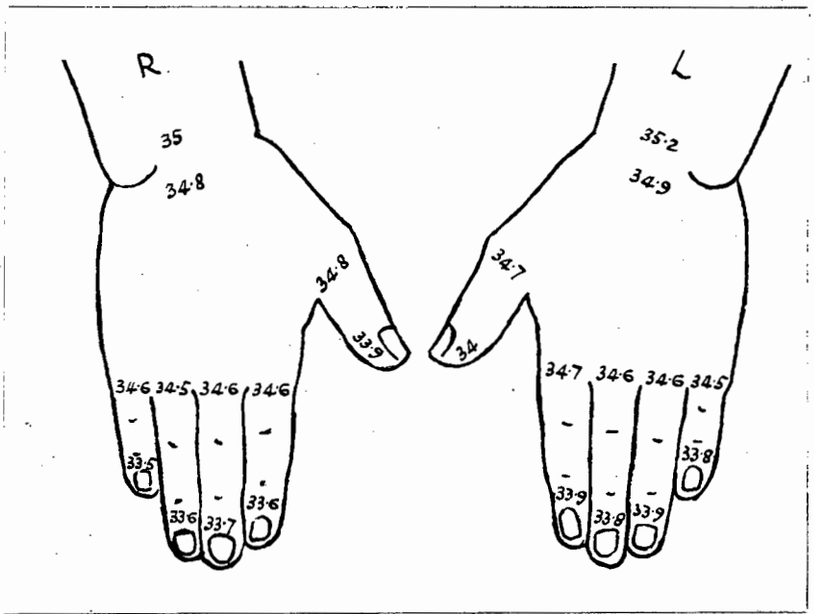


FIGURE 120. - CASE No. 16.

Skin temperature of both hands
after thirty minutes' body heating.

Before Sympathectomy.

Room temperature 21°C.

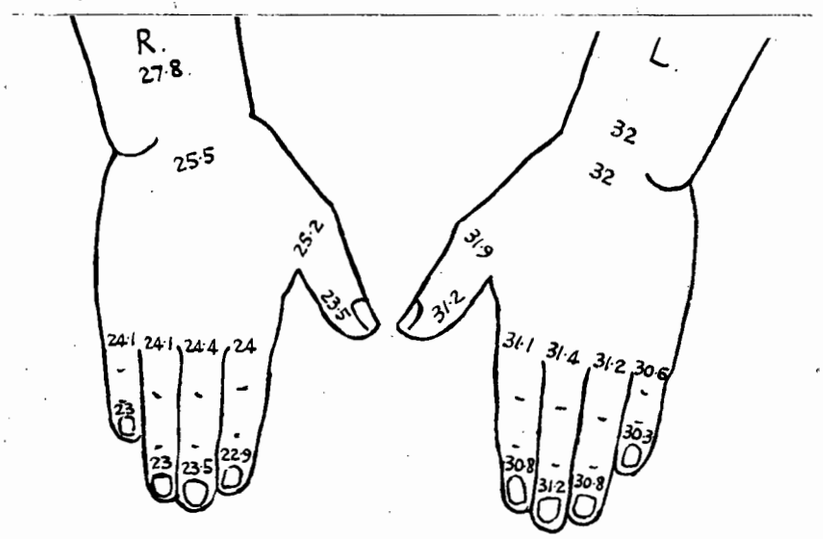


FIGURE 121. - CASE No. 16.

Skin temperatures of both hands at rest.

Left Th.2, Th.3 and Th.4 removed eight days previously.

Room temperature 20°C.

Number 17.

E.M., 47, white, male, had Buerger's Disease for seventeen years.

In 1931 in New Zealand the right leg was amputated through the mid-thigh for gangrene of the big toe.

In February, 1935, a left lumbar sympathectomy was performed in Cape Town.

In 1938, again in New Zealand, a right stellatectomy was performed for involvement of the right upper limb. A Horner's Syndrome was manifest immediately after operation. It is still present. Ever since operation he has not sweated on the right side of the face and on the right hand.

The patient has been seen at irregular intervals since 1940. His symptoms are confined to his remaining lower limb. On four occasions in the last seven years he has been hospitalised for ulceration and intermittent claudication of the left lower limb. Each time this has improved on local treatment of the ulcer, intravenous hypertonic saline and intermittent venous occlusion.

At no time has he been admitted for any specific complaint of the right upper limb.

In June, 1947, the patient was re-examined and tested to determine the integrity of the sympathetic supply to the right upper limb.

He has no occupation and exists on a charitable institution. He has a strong history of alcoholism. Since amputation of the right leg, he uses a pair of crutches.

Since stellatectomy he experiences occasional paraesthesia of the thumb of the right hand. This was present before operation and appears to be related to the use of the crutch. He has noticed, however, that the right hand is colder than the left, particularly during warm weather. The difference is not so marked during the cold weather.

The right pupil is smaller than the left. There is ptosis of the right upper lid and narrowing of the palpebral fissure.

The right hand is cooler than the left. Sweating was apparent on the left but the right hand was dry. There were several small scars on the fingers of the right hand but also several on the left. The right brachial artery was felt with considerable difficulty, a faint pulsation only being present. The left brachial artery was easily felt. The radial and ulnar pulses were only felt on the right on full dilatation and there was considerably less force than the easily palpable pulses on the left.

Skin temperature readings at rest confirm the difference on the two sides. (Figure 122. - page 316). Pulse volume readings at rest also revealed a gross difference, the right being 0.002cc., the left 0.0045cc.

/Thermo-regulatory

Thermo-regulatory body heating caused a rise in skin temperature of the right hand. (Figure 123. - page 316).

There was profuse sweating on the left upper limb and face in response to body heating but no sweating at all was apparent on the right.

Minor's Starch-Iodine test showed sweating on the left face, neck and chest. (Figure 28. - page 102). There was no sweating on the right face, neck and anterior chest wall to three inches below the clavicle where a definite margin could be seen. The hand was free from sweating.

After thermo-regulatory body heating the pulse volume of the right middle finger increased from a resting 0.0066cc. to 0.01cc.

The application of direct heat to the right hand resulted in a further increase to 0.011cc.

Pilocarpine, although producing the secretory effects, did not result in vasoconstriction.

Skin resistance measurement showed a high resistance of the right hand and forearm. The responses on both sides of the face and upper chest revealed low values. The fact that a high resistance was present means that the right hand and forearm was sympathectomised.

It was not possible to assess the integrity of the sympathetic supply to the right upper extremity purely by the plethysmographic record. Clinically, marked organic change was present. This was borne out by the failure of the pulse volume to increase following the application of direct heat to the limb.

The relative failure of the vessels to dilate on thermo-regulatory body heating may be due either to the completeness of the sympathectomy or due to the inability of the vessels to relax because of the local organic change.

Conclusions:

The persistence of the Horner's Syndrome, the absence of sweating on the right face and upper limb, both in response to thermo-regulatory body heating and to pilocarpine, the absence of fall in skin temperature following pilocarpine, and the high skin resistance following pilocarpine, all support the view that sympathectomy is complete nine years later.

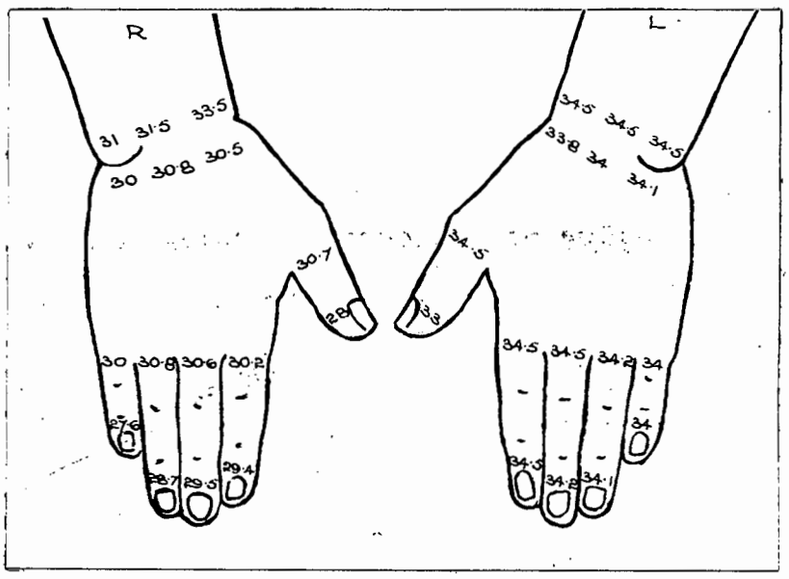


FIGURE 122. - CASE No. 17.

The skin temperatures of both hands at rest.
Right stellatectomy performed nine years previously.
Room temperature 18.7°C.

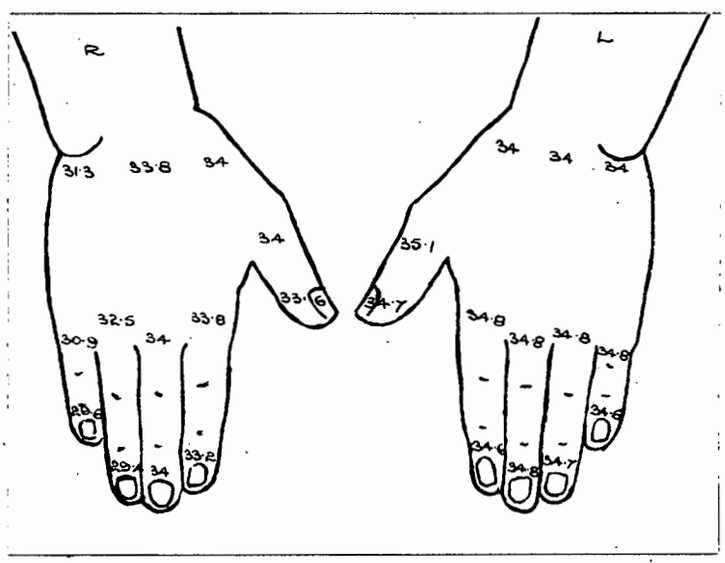


FIGURE 123. - CASE No. 17.

The skin temperatures of both hands
after thirty minutes' body heating.

Right stellatectomy performed nine years previously.

Number 18.

J.P.J., 56, white, male, received a bayonet wound in the left arm in 1915. The wound did not heal for twenty-one months. There was associated pain which was so severe as to require morphine gr.1/4 every four hours. Tolerance was acquired to morphine after six months and periarterial sympathectomy was performed.

After a further nine months Major Ackland (then at St. Thomas' Hospital, London) performed a cervico-thoracic ganglionectomy at the South African Hospital, Richmond Park. The operation was performed on 16/3/17. The immediate effect of the operation was that the arm became completely anaesthetic, and felt as if dead. The wound healed rapidly thereafter and pain was relieved. After two years sensitivity gradually returned to the arm and today there is no difference between the left and right arms.

Immediately after operation a Horner's Syndrome was present and no improvement has ever been observed.

Ever since the operation the left arm and the left side of the face have not sweated. The left hand has always felt colder than the right hand.

He never suffers from chilblains. He is easily able to distinguish between hot and cold with either hand. There is no difference in the two hands to ordinary sensations and the power of the left hand is as good as the right.

On warm days the right hand sweats profusely, whereas the left remains perfectly dry.

An extract from the operation note reveals that the sympathetic chain was cut just above the stellate ganglion, and one inch of the chain, with the second thoracic ganglion, was removed. All rami communicantes were divided. The operation was performed via the posterior approach.

The patient was first seen during 1940. It was observed that the left hand felt colder than the right. Skin temperature measurements at that time showed that the right hand was 3.7°C. higher than the left. The inner three fingers of the left hand were cooler than the thumb or index finger.

The pulse volume of the left middle finger was 0.004cc. at rest. No change occurred with multiple painful stimuli. (Figure 60. - page 228).

The left hand was dry and no sweating was observed on the face. Ptosis of the left upper eyelid and narrowing of the palpebral fissure was present. The left pupil was smaller than the right.

Three years later the patient was again tested. The clinical appearance was unchanged.

/The pulse volume

The pulse volume of the left index finger at rest was 0.003cc. After thirty minutes' body heating the volume was 0.0045cc. Again no decrease occurred in pulse volume in response to various painful stimuli.

In the second half of 1947 the patient was thoroughly tested to determine the presence or absence of sympathetic supply to the left upper extremity.

No further change had occurred in his clinical condition. The Horner's Syndrome was still present and did not hinder him at all. The left hand was colder than the right and did not sweat, although at rest all the other parts of the body were sweating profusely. Sweating was not present on the left side of the face either.

The skin temperature of the left index finger was 28.8°C. and the right 30.5°C.

The pulse volume at rest of the left middle finger was 0.0045cc. The resting pulse volume of the right middle finger was 0.035cc.

Thermo-regulatory reflex body heating was then instituted and the skin temperature of the left index finger rose from 28.8°C. to 30.1°C. The increase in skin temperature of the right index finger was only 0.5°C.

The pulse volume of the left middle finger rose to 0.012cc. A simultaneous recording of the right middle finger showed a pulse volume of 0.037cc. In both sides an increase occurred, smaller on the right, but it must be remembered that the right middle finger was practically fully dilated at the onset of the test. (Graph 28. - page 226).

The left hand was then placed in a water bath at 45°C. and retained there for ten minutes. The pulse volume, after the application of direct heat, rose to 0.024cc. This ability to dilate further is indicative of absence of organic change in the vessel, as would be suspect from the figure obtained from reflex body heating. (Figures 1. and 2. - page 67).

The digital volume of the left middle finger increased by 2.5cc. in response to body heating. The right middle finger volume increased by 0.25cc.

Little or no change occurred in the pulse rate in response to body heating.

The skin resistance, as estimated on 22/8/47, showed that the whole of the left upper extremity had a high resistance. High resistance to the passage of an electrical current was also present on the left forehead and cheek. The resistance was low on the left lower jaw and left side of the neck to a line about one inch above the clavicle. Resistance on the right side of the body was low. The line of demarcation between the areas of high and low resistance was in the middle line and could be sharply drawn. (Figure 53. - page 146).

/Minor's

Minor's Starch-Iodine sweating test was performed on this patient on 30/9/47. After thirty minutes' body heating sweating was profuse on the right side of the forehead, face and upper lip. There was profuse sweating on the whole of the right upper extremity and right side of the chest. Sweating also occurred in the left axilla and below a line about one-and-a-half inches above the left nipple. Posteriorly, sweating occurred over the whole of the right side of the back and below a line drawn from the seventh cervical spine to the left axilla. (Figures 29. and 30. - pages 103 and 104).

Sweating was completely absent on the left upper extremity, except for the axilla and an area on the medial and posterior aspect of the left arm. Sweating was completely absent on the left side of the neck, left face and left shoulder.

The line of demarcation between sweating and non-sweating areas was well defined.

On 9/9/47 the patient received pilocarpine gr.1/6 intramuscularly. Continuous plethysmographic recordings were made of both middle fingers. (Graph 10. - page 174). The pulse volume of the left middle finger at rest was observed for over thirty minutes. Very little change occurred in the height of the volume which averaged 0.004cc. It is thus apparent that the pulse volume appeared standardised before the administration of pilocarpine. No change in the height of pulse volume was apparent at the moment of injection.

Nine minutes after injection an increase in the height of pulse volume was apparent. The pulse volume was 0.006cc. The increase in the size of the pulse was maintained. Nineteen minutes after injection, the pulse volume was 0.0075cc. Thirty minutes later the reading was 0.009cc. Although at several points the reading was 0.010cc., the mean volume at the termination of the test, fifty-two minutes after the administration of pilocarpine, was 0.009cc.

The pulse volume of the normally innervated right middle finger showed considerable fluctuation. At rest the pulse volume varied between 0.029cc. and 0.017cc. At the moment of injection of pilocarpine, the volume decreased sharply to 0.011cc. (Figure 124. - page 322). This was followed by a rapid return to and over the previous maximum level. The volume reached 0.032cc. The fluctuation in the pulse volume persisted but the average volume appeared slightly higher than before injection. This increase persisted for about ten minutes, following which the curve took a gradual downward trend. Whereas before injection the average pulse volume was between 0.029cc. and 0.017cc., forty minutes later it was between 0.023cc. and 0.014cc. - a tendency to vasoconstriction.

The digital volume, whilst showing an increase of nearly 0.2cc. in thirty-eight minutes in the left middle finger, increased 0.7cc. in fifty minutes after pilocarpine.

Whilst an increase in the digital volume of the

/right middle finger

right middle finger was apparent before pilocarpine, a decrease occurred after injection. The changes present are, however, slight.

The skin temperatures of both index fingers were recorded at regular intervals. The left finger initially was 25°C. Shortly before the injection of pilocarpine the plateau of the curve appeared to have been reached. The highest reading before injection was 28.7°C. Ten minutes after pilocarpine the temperature had risen to 30.2°C. Thereafter variation occurred between 30°C. and 30.7°C.

The right or non-sympathectomised finger had an initial temperature of 29.5°C. This rose to 30.8°C. before pilocarpine. After injection the temperature varied between 30.8°C. and 31.5°C. No gross rise occurred following pilocarpine intramuscularly.

Whereas in other patients the effect of pilocarpine on the secretions was manifest within a few minutes, twelve minutes elapsed before salivation or sweating occurred. Sweating was observed to be present on the right face and upper extremity but no sweating at all occurred on the left upper extremity or left face. Sweating was present in both axillae.

The effect of a deep breath on the pulse and digital volumes is seen in Figure 58. (page 227).

Both middle fingers were recorded simultaneously. At the outset the right (normally innervated) finger is the upper. The respirations are noted above. At the moment of the deep breath the digital volume of the right middle finger appeared to rise slightly. This was followed by a marked decrease in digital volume - the right now becomes the lower tracing. At the same time, there is a marked reduction in pulse volume from 0.04cc. to 0.013cc.

The volume of the pulse of the left middle finger (sympathectomised) was 0.022cc. before a deep breath and 0.024cc. at the corresponding point of the right middle finger.

Whilst both hands were well dilated, both feet were immersed in ice water. The responses are observed in Figure 62. (page 229). The right (normal) middle finger is recorded on the upper tracing at first. The signal indicates the point at which immersion occurred. Immediately, a constriction took place, as judged by the fall in digital volume. A fall of 1.8cc. occurred in the space of twelve seconds. The pulse volume decreased from 0.041cc. to 0.011cc.

The left middle finger (sympathectomised) is the lower tracing at first. On immersion of both feet in iced water, the digital volume did not vary at all. The pulse volume before immersion was 0.018cc. and, after immersion, was still 0.018cc.

The response to immersion was repeated. The pulse volume of the left middle finger actually increased

/slightly

slightly from 0.02cc. to 0.022cc. following immersion of both feet in iced water.

The right middle finger again constricted following immersion. The pulse volume decreased from 0.019cc. to 0.010cc. The digital volume, too, decreased, although the decrease is not as marked as when the vessels were better dilated.

This patient is, perhaps, the longest post-sympathectomised individual reported. The management of the case from the onset deserves every credit. Following a bayonet wound of the left arm, the patient developed intractable causalgia which did not respond to conservative measures. Six months later periarterial sympathectomy was undertaken. Not unexpectedly, it was of no avail. Then, after nine months, through a difficult approach, the stellate ganglion and the sympathetic chain to below the second thoracic ganglion were removed, following section of all the connecting rami. This took place seven years before Royle's observations were published!

When examined thirty years later, this patient is as completely sympathectomised as immediately after operation. This is borne out by the following features:-

(1) Presence of the Horner's Syndrome.

(2) Absence of sweating in the sympathectomised areas, as brought out both by reflex body heating and after pilocarpine injection.

(3) Failure of the vessels to dilate on reflex body heating. That this failure is not due to any organic change, is shown by the ability of the vessels to dilate on the application of direct heat.

(4) A high resistance is present to the conductivity of an electrical current.

(5) Reflex vasoconstrictors, such as a deep breath and the immersion of both feet in iced water, are without effect on the pulse and digital volume of the sympathectomised digit. The striking contrast between the sympathectomised and normally innervated hand is brought out.

Thus there has been no return of sudomotor or vasomotor function in a limb sympathectomised thirty years ago.

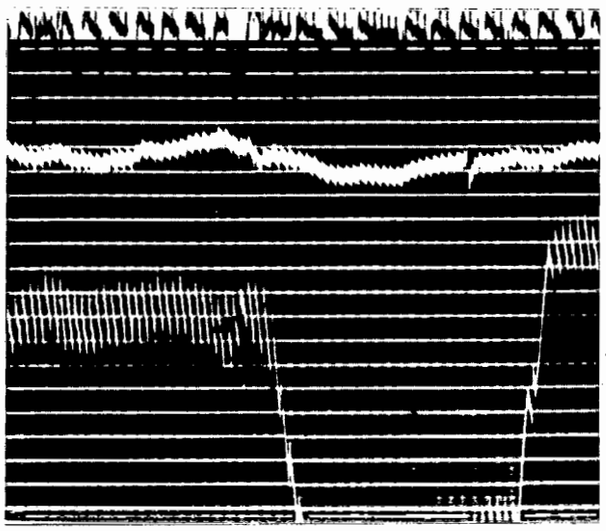


FIGURE 124. - CASE No. 18.

The left middle finger (upper tracing) and right middle finger at the moment of injection of pilocarpine.

Thirty years after removal of left stellate and second thoracic ganglia.

V. EXPERIMENTAL INVESTIGATIONS.

The vast majority of experimental work on the Sympathetic Nervous System has been done on animals which do not bear a close resemblance to man; rabbits, rats, mice, cats and dogs have all been used. The animal of choice for the present experimental investigations was the rhesus monkey.

This monkey, although small, is readily handled and is easy to keep under observation. The animal's salient feature, however, is the close similarity of its sympathetic nervous system to that of Man.

(a) ANATOMY AND PHYSIOLOGY.

In human anatomy it is customary to regard the thoracic sympathetic trunk as generally comprising eleven or twelve ganglia set in relation to the thoracic vertebra, and separated, by the diaphragm, from the abdominal or lumbar chain, whose ganglia are in relation to the lumbar vertebrae.

Radiographs of the vertebral column in five specimens of this series bear out the great similarity between the vertebral column in the rhesus monkey and in the human. No difference was observed in the number of cervical vertebrae. Normally, both man and monkey possess seven cervical vertebrae. At first sight, there appears to be eight cervical vertebra, both in the antero-posterior and lateral views - on careful enumeration, however, the actual number is seven. Special views of the cervical spine were taken in subsequent specimens. (Figure 125. - page 326, Figure 126. - page 327, and Figure 127. - page 328). Confirmation of the presence of

/seven cervical

seven cervical vertebrae was thus obtained.

No variation of the total number of thoracic vertebrae occurred. There were twelve thoracic vertebrae, as judged by the presence or absence of a rib, in each of the specimens examined. In these animals there appeared to be either two or three floating ribs. The analogy between the human and the monkey thus is drawn even closer.

In each of the five animals radiographed there were either six or seven lumbar vertebrae. In these specimens there appears to be either "lumbarisation" of the first sacral segment or "sacralisation" of the last lumbar vertebra. (Figures 128., 129., 130., 131., 132., 133., 134. -- pages 329, 330, 331, 332, 333, 334, 335).

Therefore, as far as the number of the cervical and thoracic vertebrae are concerned, the monkey corresponds exactly with that of the human. It would be a natural conclusion, therefore, that the sympathetic nervous system of the cervical and thoracic regions should be identical in both the monkey and in the human being.

According to Zuckerman, however, a corresponding description of the sympathetic chain in the rhesus monkey and the human, would be misleading, for in the normal animal with twelve rib-bearing vertebrae, the first lumbar vertebra (and frequently part of the second) is without exception intra-thoracic in position. This thirteenth post-cervical vertebra and its nerve should be regarded as a fixed point that marks the cranial limit of the lumbar plexus, whether or not it is rib-bearing and irrespective of the number of non-rib-bearing lumbar vertebrae.

In thirty-three out of forty-eight specimens

/Zuckerman

Zuckerman observed an extra rib. This thirteenth rib ranges in size between 1cm. and 7cm. The right and left thirteenth ribs are frequently unequal and, in such cases, the right is always longer. An extra rib may be present on one side only.

In none of the animals of this series was a thirteenth rib demonstrable radiologically. In any case, the presence of a thirteenth rib should not materially affect the arrangement of the sympathetic supply to the upper extremity.

Zuckerman was able to recognise a definite anatomical plan but noted the variability of the sympathetic nervous system of monkeys. Basically all specimens of this series agreed with each other but, as Zuckerman states, even bilateral symmetry is unusual in any one animal.

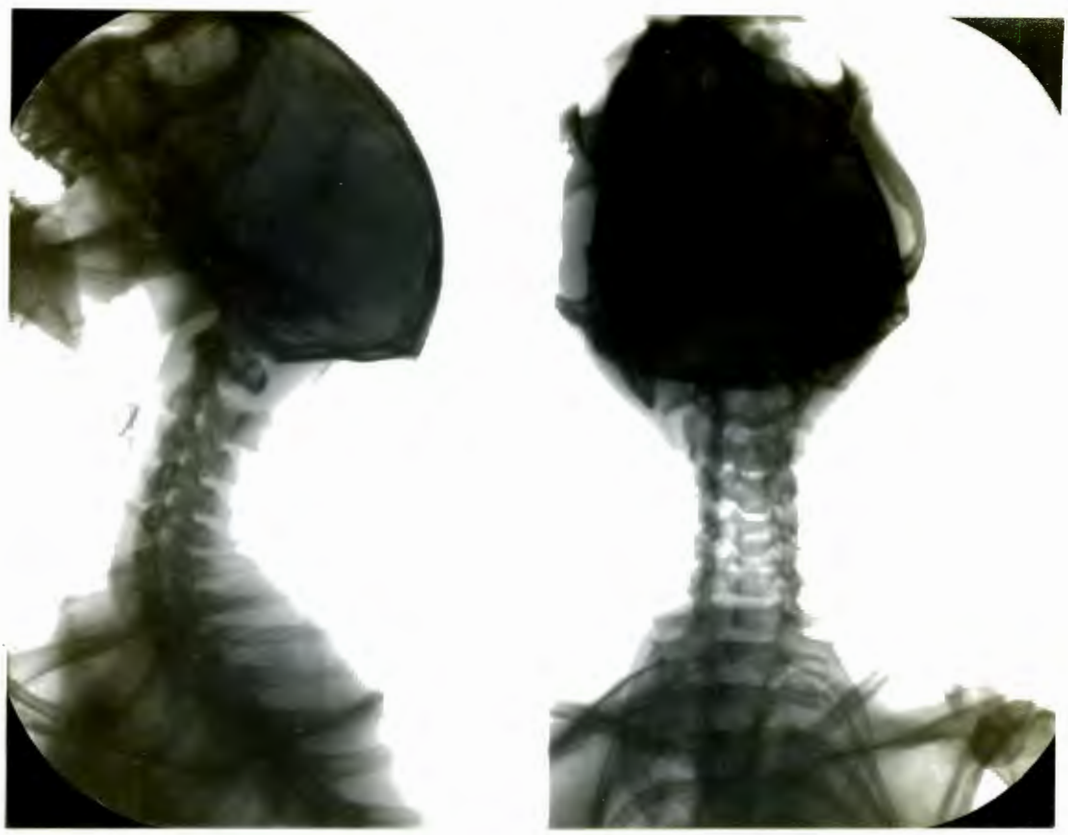


FIGURE 125. - "B"

Lateral and antero-posterior views of cervical spine showing seven vertebrae.

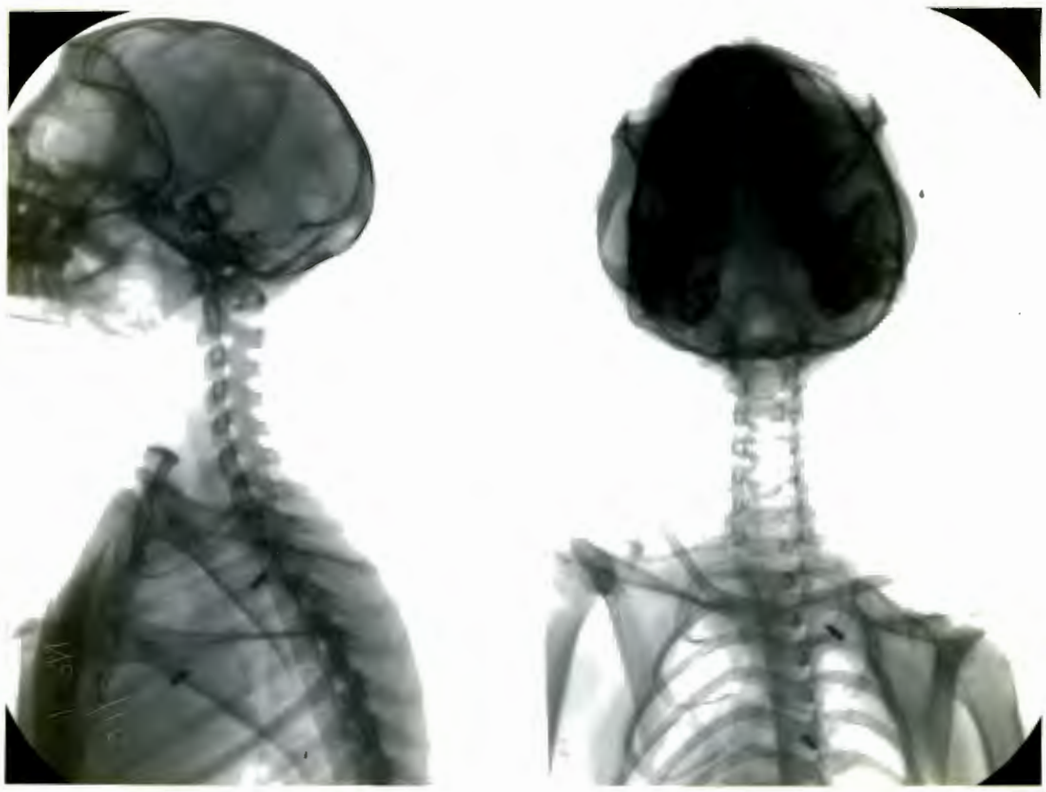


FIGURE 126. - "D".

Antero-posterior and lateral views of cervical spine showing seven vertebrae.

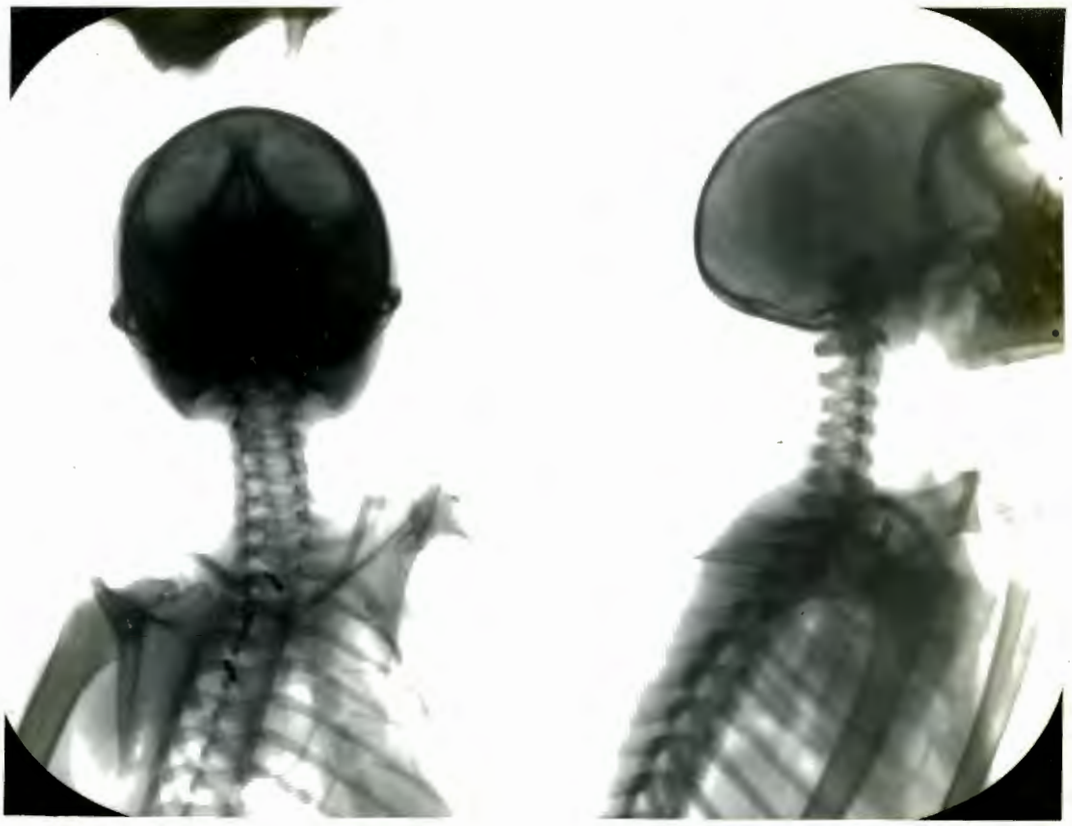


FIGURE 127. - "G".

Antero-posterior and lateral views of cervical spine showing seven vertebrae.

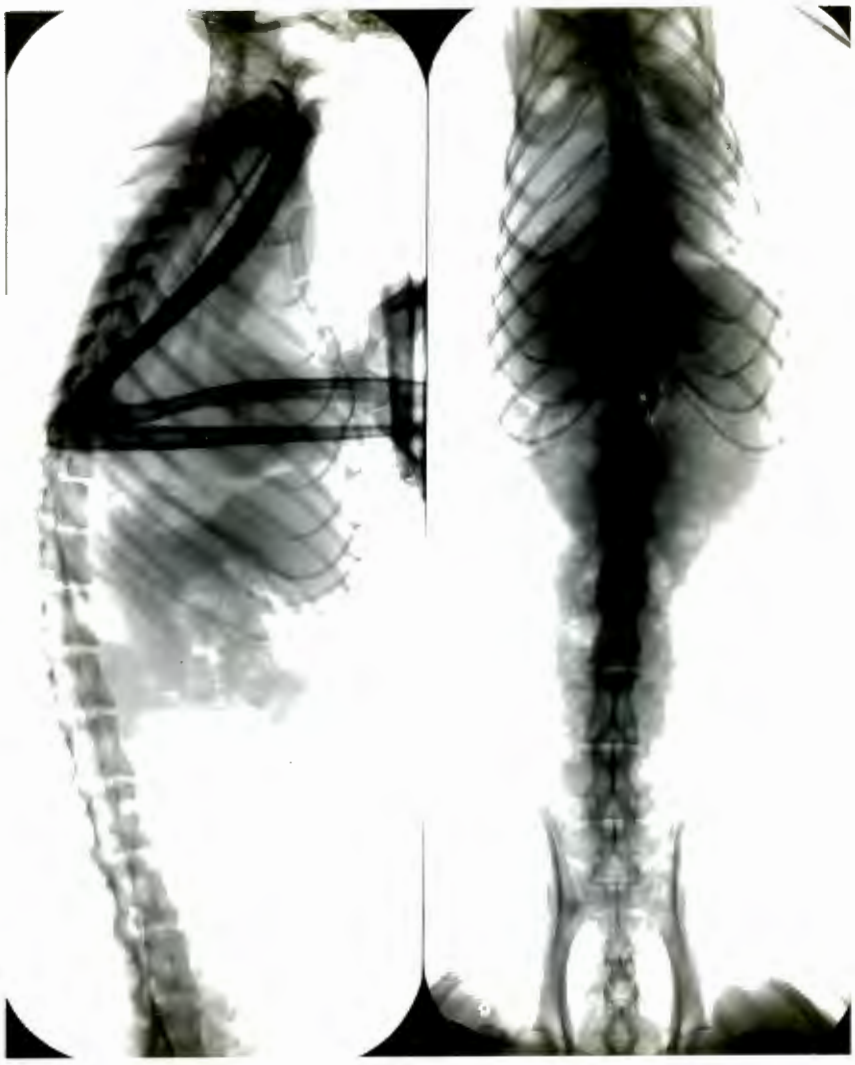


FIGURE 128. - "B".

Lateral and antero-posterior views showing the composition of the thoracic and lumbar spine.

FIGURE 129. - "D".

Antero-posterior and lateral views showing the composition of the vertebral column.

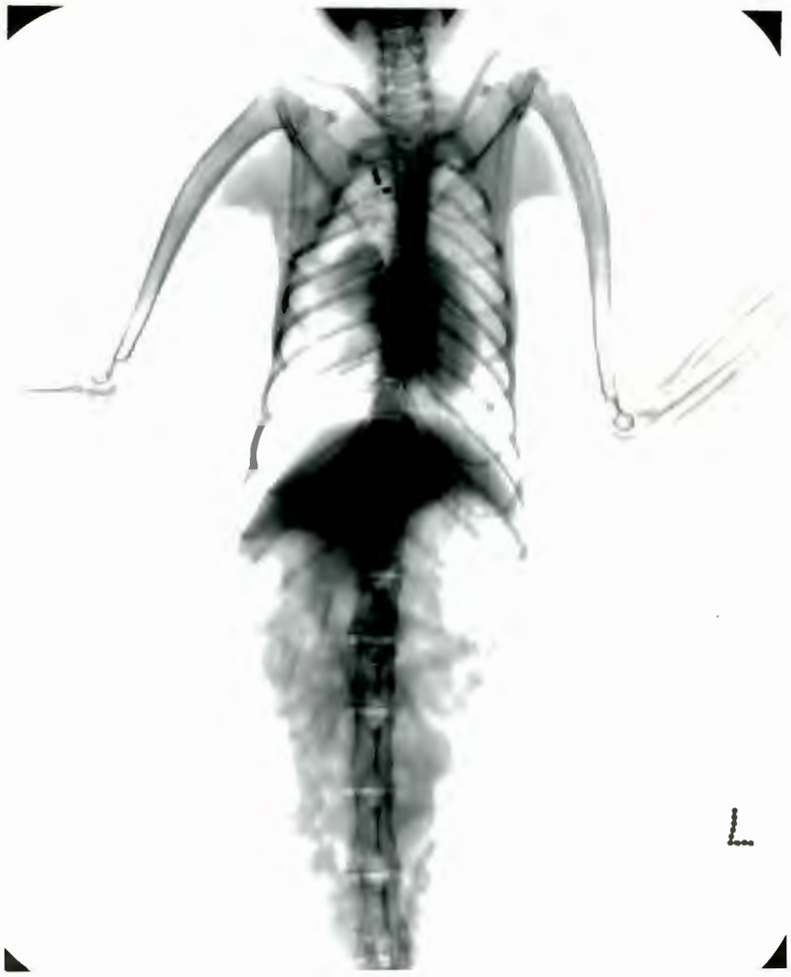


FIGURE 130. - "E".

Antero-posterior view showing the number of rib-bearing thoracic vertebrae.

FIGURE 131. - "E".

Lateral view of vertebral column.

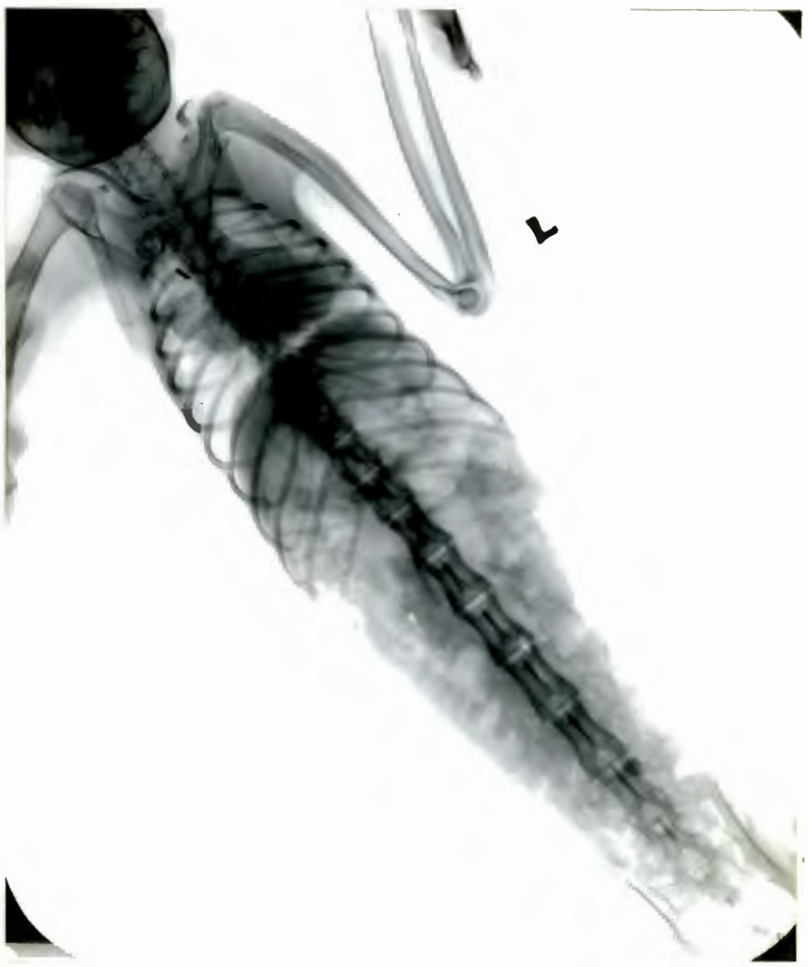


FIGURE 132. - "F".

Antero-posterior view showing composition of thoracic and lumbar spine.

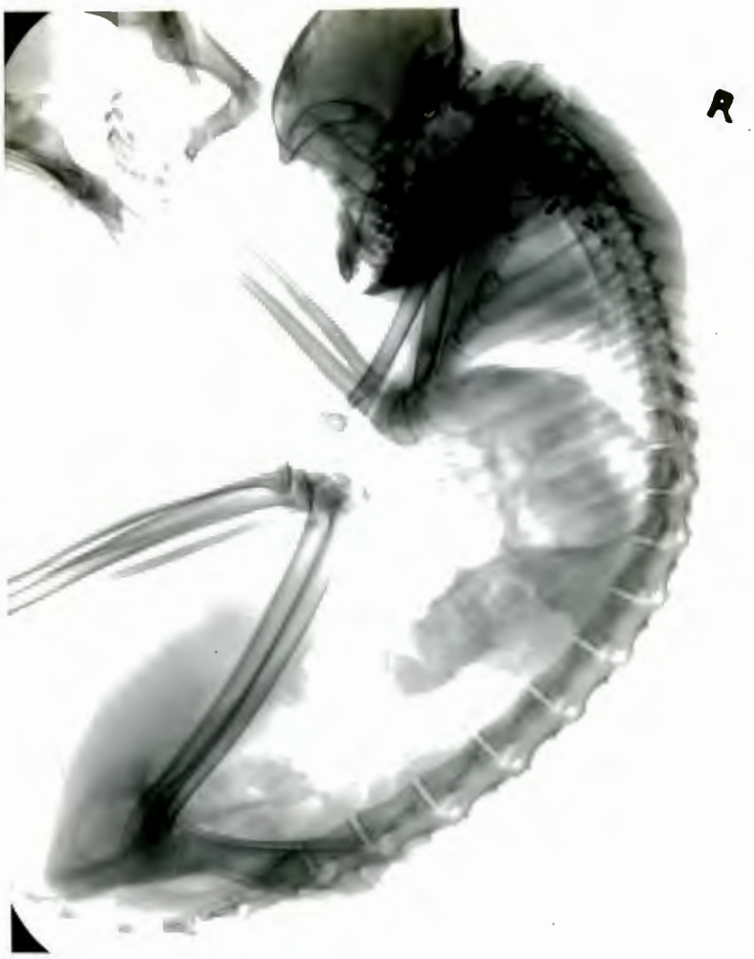


FIGURE 133. - "F".

Lateral view of vertebral column.

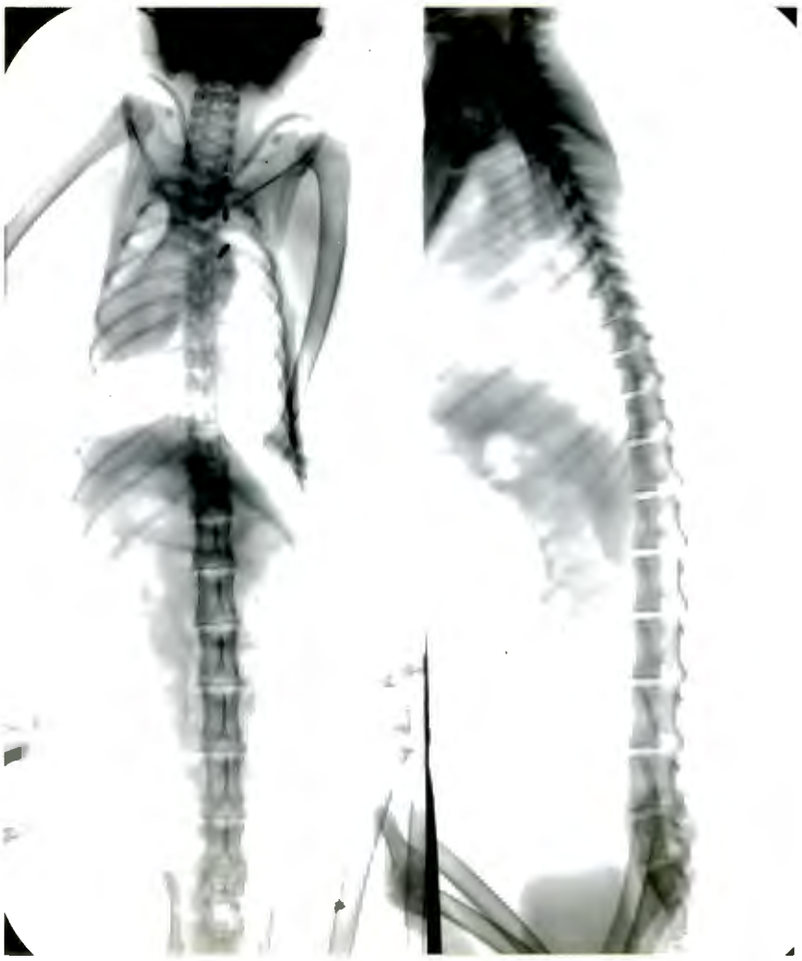


FIGURE 134. - "G".

Antero-posterior and lateral views showing the composition of the vertebral column.

In this series of rhesus monkeys the cervical sympathetic chain was so intimately associated with the vagus nerve as to be considered as one trunk. However, the two components could be separated easily throughout the whole length of the course. In "G" the vago-sympathetic trunk was one structure and the sympathetic and vagus could not be separated from each other. The sympathetic trunk was apparently continuous with the vagus below but, on stimulation, dilatation of the pupil resulted. Only thus were the sympathetic components of the trunk recognised. This close association of the vagus nerve and the sympathetic chain was confirmed by the numerous anastomoses existing between their cardiac branches and the recurrent laryngeal nerve. After dissection the sympathetic chain usually could be recognised lying posterio-medial to the vagus nerve. Zuckerman (1938) also noted the close association of the vagus and the sympathetic in the cervical region of the rhesus monkey. He found also that the anastomotic network of one side may communicate with that of the other. Funaoka and Shinosaki (1938) found that communications between the human vagus and cervical sympathetic chain are more mumerous on the right side than on the left. With this Zuckerman agrees and notes that the same appears to be true for the monkey.

In most laboratory animals the cervical sympathetic chain is distinct from the vagus. In the dog, however, the sympathetic and the vagus are intimately united within a single sheath and it is extremely difficult to separate the two (Sisson - 1917, Sonntag - 1923). There is an extensive intercommunication between the vagus and the sympathetic trunk where they run separately.

In the dissected specimen in Figure 135. (page 341) the superior cervical ganglion is an oval, elongated flattened

/structure

structure at the base of the skull lying in close relationship to the vagus nerve. The ganglion lies postero-medial to the vagus and so intimate is its contact with the vagus, that blunt dissection is necessary to define the two structures. The internal carotid artery lay anterior to the ganglion and, as it entered the carotid foramen on its way to the cranial cavity, the sympathetic accompanied it.

Medially, fibres from the superior cervical ganglion run to the carotid sinus and fibres accompany the superior laryngeal nerve which crosses the lower part of the ganglion. Laterally, branches are distributed to the contituents of the cervical plexus.

Tracing the sympathetic trunk caudally, no definite ganglia are demonstrable. The first suggestion of a ganglion is at the subclavian artery where the middle cardiac nerve appears to arise. At this point a slight thickening is present.

Viewed from within the pleural cavity, the stellate ganglion is seen to be a crescentic body shining through the parietal pleura. (Figure 136. - page 342). It is about 7.5. - 10mm. long and extends from the neck of the second rib to the neck of the first. Its concavity faces medially and caudally, and the superior intercostal vessels separate it from the first thoracic nerve. In the dissected specimen it is seen to lie posterior to the subclavian artery, which, in Figure 135. (page 341) has been displaced medially to demonstrate the ganglion and its rami communicantes.

The middle cervical ganglion is not a definite structure in this specimen. It is connected to the stellate ganglion by the two limbs of the subclavian loop. It was recognised as such by the fact that the middle cardiac nerve,

/took origin

took origin at a point just cranial to the junction of the two subclavian loops.

In Figure 135. (page 341) the second thoracic ganglion appears to be incorporated in the inferior horn of the stellate ganglion. A definite but narrow waist or constriction, however, could be seen separating the two. Zuckerman found that in sixteen of twenty-two specimens the inferior horn of the stellate ganglion included the ganglion of the second space.

The branches of the stellate ganglion are conveniently divided into a medial and a lateral group. The lateral group comprises grey rami communicantes to the first thoracic nerve, eighth cervical nerve and to the seventh cervical nerve and a grey ramus accompanying the vertebral artery.

A grey ramus to the sixth cervical nerve has occasionally been demonstrated by Zuckerman, who also considered that, when the second thoracic ganglion is incorporated within the stellate complex, its rami communicantes can be regarded as branches of the stellate.

White and grey rami communicantes are given off to both the first thoracic nerve and to the communicating branch between the second and first thoracic nerves.

On the lateral side of the stellate there appears to be a ramus communicans dividing into two branches - one to the first thoracic nerve and the other to the second thoracic nerve. It passes over the neck of the second rib. This is the communicating branch between the second and first thoracic nerves. Zuckerman found it to be a well-defined branch of the second thoracic nerve in nineteen of twenty-eight animals. In most of these cases the stellate ganglion extended sufficiently far caudally to incorporate the second thoracic ganglion. In almost each of his cases the arrangement of the rami communicantes of the upper two thoracic nerves suggested that, even when no separate branch connected these two nerves themselves,

/fibres

fibres yet passed by way of the stellate ganglion from the second to the first thoracic nerve, and thence to branches of the brachial plexus. The communicating branch may be closely applied to the lateral aspect of the stellate ganglion.

When a distinct communication passes from the second to the first thoracic nerve, it may receive one or two rami communicantes from either, or from the caudal and cranial parts of the stellate ganglion. Sometimes the only sympathetic fibres to the communicating branch pass via the grey ramus of the second thoracic nerve (Zuckerman).

The grey rami communicantes to the seventh and eighth cervical nerves appear to take origin from the stellate ganglion by a common trunk which arises as a supero-lateral extension of the body of the stellate. This common trunk is also the pathway by which the fibres which pass with the vertebral artery go to form the vertebral plexus. In this specimen a definite branch seemed to accompany the vertebral artery, from the stellate ganglion. It is interesting in view of the fact that Botar (1932) states that this "vertebral" trunk is the true cervical part of the sympathetic chain. He says that in man and the anthropoids it continues to give deep communicating branches to each cervical segment, except the first.

The medial group of branches of the stellate ganglion includes the inferior cardiac nerve, seen running downwards and medially, closely related to the subclavian artery, to the deep cardiac plexus, and the two loops around the subclavian artery, which unite above the artery to form the cervical sympathetic trunk. The inferior cardiac nerve is intimately connection with the recurrent laryngeal nerve.

/The second thoracic

The second thoracic ganglion is a well-defined structure lying in the space below the neck of the second rib. It is separated from the stellate by a narrow but definite constriction. It is connected to the second thoracic nerve by a short but relatively thick ramus, probably incorporating both grey and white rami communicantes. This ramus enters the nerve just medial to the point at which the communicating branch to the first thoracic nerve is given off. On the medial side a fibre is seen running from just below the second thoracic ganglion to the cardiac plexus.

The third thoracic ganglion lies in the third interspace. The ramus to the thoracic nerve is surprisingly large. There is no obvious communication between the third and second thoracic nerves.

Tracing the sympathetic trunk caudally, the third to the seventh ganglia are situated in the middle of their respective spaces and are connected to their corresponding intercostal nerves by short white and grey rami communicantes which are either wholly conjoined or connected together at their ganglionic or intercostal nerve extremities.

FIGURE 135.

Dissection of the
Left Cervical and Thoracic Sympathetic Trunk.

a.	..	Cervical plexus	g.	..	Vertebral artery
b.	..	Int. Jugular vein	h.	..	Subclavian artery
c.	..	Vagus	i.	..	Stellate ganglion
d.	..	Phrenic nerve	j.	..	Pulmonary artery
e.	..	Sympathetic trunk	k.	..	Root of left lung
f.	..	Brachial plexus	l.	..	Descending aorta

FIGURE 136.

The left sympathetic trunk viewed from below towards the apex of the pleura.

The Sympathetic Supply to the Upper Extremity.

The sympathetic supply to the upper extremity in the monkey was mapped out by electrical stimulation of the sympathetic chain.

The stimulator employed throughout this series of experiments was the Ediswan Electronic Nerve Stimulator (Ritchie B.N.I.). The amount of current passed through the electrodes was 2 volts at a frequency of 50 cycles per second, and a duration of 10 milliseconds.

The electrodes supplied with the instrument were found to be too large for the work necessary on the sympathetic nerves. Electrodes were thus constructed of two silver pins. These were mounted on a curved glass rod and well insulated. The points of the pins were filed down so that no trauma could be produced by the application of sharp points. The distance between the points was 1mm. The glass rod was curved in order to have easy access to the sympathetic chain in the depths of the wound. All that was necessary was the application of the silver points to the sympathetic nerve.

A long flex, insulated in plastic, was connected to the instrument. This flex and the glass holder were easily sterilised either by boiling or by autoclaving. The instrument was tested on each occasion, before sympathetic stimulation, by touching the pectoralis major. A muscular contraction at the site indicates the passage of the current.

The stimulator, when applied to the sympathetic chain, causes an immediate fall in the volume of the hand and a marked diminution in the height of the pulse volume. (Figure 137. - page 347).

Such was the sensitivity of the instrument that,

/when an attempt

when an attempt was made to stimulate the sympathetic chain through the overlying intact pleura, no response ensued. The chain and ganglia had to be stimulated directly. The sympathetic trunk was thus freed by blunt dissection and elevated on a blunt hook. Crushing by the application of forceps, was avoided for fear of interrupting the conductivity of the current.

After vasoconstriction had been demonstrated by stimulation of the stellate ganglion, stimulation of the chain and ganglia was carried caudally in an attempt to define the lowermost extent of sympathetic supply to the upper extremity. This was carried out routinely in all specimens before sympathectomy was finally performed.

In three of the specimens, "A", "B" and "E", the sympathetic supply to the upper extremity was found to be from the stellate to the lower margin of the fourth rib. Stimulation caudal to this point did not cause vasoconstriction in the hand. In specimens "D", "F" and "G" the upper extremity was supplied by fibres extending only as low as the third thoracic ganglion. Specimen "C" was unusual in that stimulation of the third thoracic ganglion had no effect on the pulse or hand volume, yet when the fourth, fifth and sixth ganglia were stimulated vasoconstriction resulted.

As judged by vasoconstriction produced by electrical stimulation of the sympathetic trunk and ganglia, the upper extremity of the monkey was supplied by the stellate and second and third thoracic ganglia in three specimens, by the above and the fourth thoracic ganglion in three specimens. In one specimen the outflow extended as far caudally as the sixth thoracic ganglion, but no response occurred on stimulation of the third thoracic ganglion in this specimen.

/(Figure 138.

(Figure 138. - page 348).

The sympathetic supply to the pupil was noted at the same time that the changes in the pulse volume were recorded. Normally, stimulation of the sympathetic fibres to the pupil results in dilatation. At the time of stimulation the pupil was thus observed. In all specimens dilatation of the pupil resulted from application of the electrodes to the stellate ganglion. In no animal did stimulation of any part of the sympathetic system caudal to the stellate ganglion result in dilatation.

A further significant feature was observed in specimens "A", "B", "C" and "E". On stimulation of the stellate ganglion, in addition to vasoconstriction and dilatation of the pupil, a definite increase in the heart rate occurred. Stimulation caudally also produced an increase in heart rate. But a point was usually reached at which, although vasoconstriction may occur, there was no increase in heart rate. Thus in "A" a further tachycardia occurred with the fourth thoracic ganglion but not on stimulation of the fifth thoracic ganglion. In "B" there was an increase in heart rate from 110 to 120 and in "E" stimulation of the second thoracic ganglion increased the rate from 165 to 195.

This observation was particularly obvious in "C". On stimulation of the stellate ganglion an obvious quickening of the heart rate could actually be seen at the time of operation. This increase in heart rate was reproduced by stimulation of the sympathetic chain as far caudally as the fourth thoracic ganglion. At this level there was an increase in rate from 110 to 135. Stimulation of the sixth thoracic ganglion produced vasoconstriction in the hand, but no effect on the rate

/of the heart

of the heart.

Although it was not actually plotted, the sympathetic supply to the heart, whether direct or indirect, could be determined by this method of stimulation.

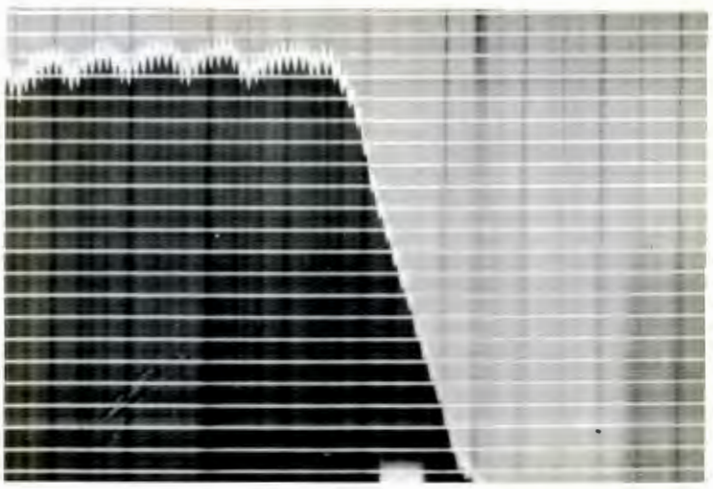


FIGURE 137. - "E"

Vasoconstriction resulting from
stimulation of the
fourth thoracic ganglion.

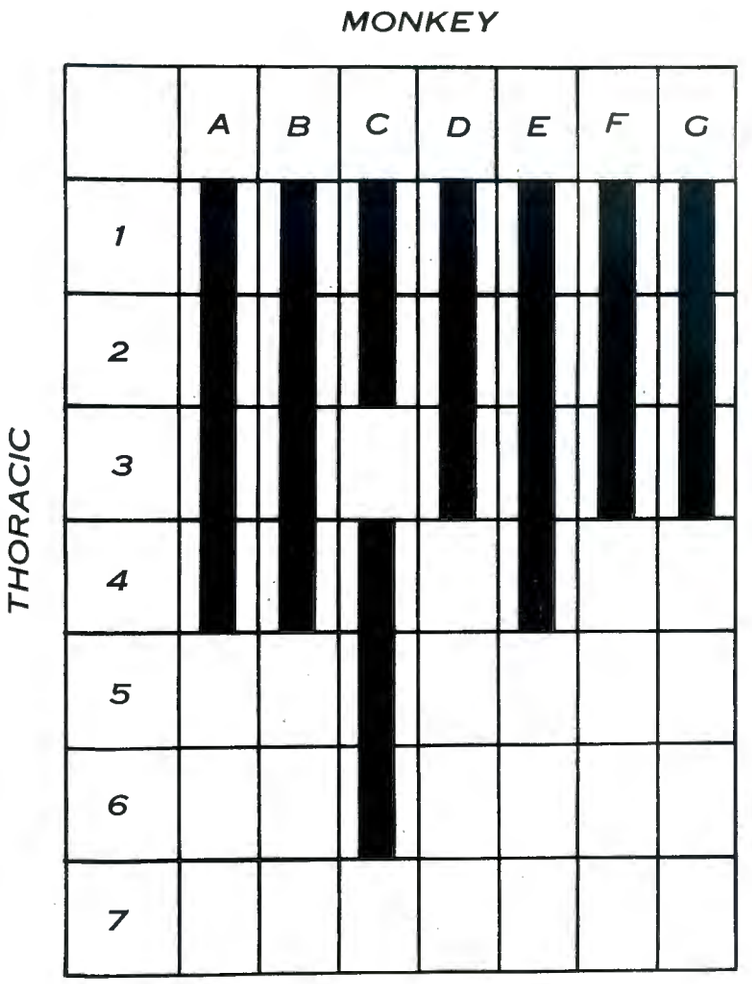


FIGURE 138.

Schematic representation of the sympathetic supply to the upper extremities in rhesus monkeys, as obtained by stimulation of the sympathetic ganglia.

(b) OPERATIVE PROCEDURE AND POST-OPERATIVE COURSE.

The Monkey was placed in a wire cage, about 3' x 2' x 1'. A hind limb was grasped and no difficulty was obtained in defining the short saphenous vein on the calf of the leg. The overlying hair was shaved and, using a fine needle, the vein was entered. A 2.5% solution of sodium pentothal was then injected intravenously. Depending on the size of the monkey, it was found that 1cc. was sufficient to render it asleep. A further 1cc. was then administered. It has been unnecessary to use more than this amount of sodium pentothal and, should more have been used, it was noted that post-operative return to consciousness was delayed.

The monkey, now soundly asleep, was removed from the cage, and washed in warm water. It was then placed on the operating table and anaesthesia continued. Depending on the depth of anaesthesia, an endotracheal tube was passed by direct laryngoscopy and anaesthesia maintained by small doses of trilene or ether, and nitrous oxide and oxygen. Should the initial plane of anaesthesia not be sufficient to enable the passage of the endotracheal tube, ethyl chloride spray on a Schimmelbusch mask was administered until the plane was sufficiently deep. The nasopharynx was packed off with gauze so that positive pressure could be applied. The operation was conducted mainly under controlled respiration by the anaesthetist.

The anterior chest wall was then shaved and an area was prepared extending from above the clavicle, superiorly, down to the fifth or sixth rib, inferiorly, and from the axilla and shoulder joint to the opposite parasternal margin lateromedially.

/The wrist and

The wrist and lower half of the forearm, of the side to be operated on, was shaved and a layer of vaseline applied. The hand was then placed in a plethysmograph tube and the tube sealed with vaseline. A recording was then made before any operative procedure was undertaken.

The monkey was placed in the supine position and maintained thus with the aid of several sandbags. Sterile towels were draped over the animal so that only the field of operation was exposed. Sterilised instruments and towels were used throughout and the strictest asepsis practised.

The skin incision was placed over the third rib and extended from the anterior axillary fold laterally to the sternal margin medially. The initial skin incision was carried through the superficial fascia on to the pectoralis major which was then divided in the line of its fibres. Pectoralis minor was dealt with in a similar manner.

The periosteum over the third rib was incised and the third rib removed subperiosteally from the axilla to the sternum. The cartilage of the second rib was divided or the second rib removed in a like manner to the third.

The pleura was incised and the lung gradually collapsed. The anaesthetist, however, was able to inflate or deflate the lung at will with the aid of positive pressure.

The internal mammary vessels were caught at the medial margin of the wound, divided and ligated.

The wound was then spread digitally and a self-retaining retractor inserted. A small Doyen's mouth gag was found to be the best retractor.

The lung was free of any pathology in six specimens. In "A" the apex was found to be adherent. On attempting to

/divide the

divide the adhesions, a cavity was entered - extrapulmonary - which contained a creamy, string-like material (culture was sterile - no cells were seen on microscopy). The "cyst" was dissected free and removed completely.

The sympathetic trunk could be easily seen through the parietal pleura. After localisation of the various ganglia, an attempt was made to stimulate the trunk and ganglia through the intact pleura. No response was noted either plethysmographically or by observation of the pupil.

The pleura was then incised over the sympathetic trunk and the ganglia and rami communicantes defined by blunt dissection, care being taken not to apply any form of crushing to the ganglia or to the chain. The chain, ganglia, and rami having been defined from the stellate ganglion to the fifth thoracic ganglion, the trunk was elevated on a blunt hook, the stimulator applied and a plethysmographic record taken.

The caudal limit of the sympathetic supply to the upper limb was determined by stimulation. The trunk was divided just below this point and the sympathetic chain dissected free to a point just above the second rib and this portion removed. The bed was stimulated at several points to ascertain whether any stray sympathetic fibres had been left intact. Particular care was taken not to injure the intercostal vessels as they ran under the trunk. Except in "B" the intercostal vessels all ran posterior to the chain. The cut ends of the sympathetic trunk were left as they lay when divided. No attempt was made to bury them in muscle, nor were any clips or cylinders applied over the ends.

All bleeding points were checked and the pleura closed without drainage. The lung was fully expanded by

/Positive pressure

positive pressure before the last suture was inserted and 100,000 units of penicillin were instilled into the pleural cavity. The pectoralis major and minor were sutured in layers, using chromicised gut. Silk sutures were used for the skin. A dressing was placed in position and the anaesthetic discontinued.

The time taken to recover from anaesthesia varied. For the most part the animals were sitting up within three hours of completion of the operation. Within twelve hours they were eating normally and moving around freely. There was no apparent restriction of movement of the limb on the operated side.

The wounds all healed by primary intention. The animals never touched the wounds at all. The skin sutures usually came out spontaneously about 6 - 8 weeks after operation.

Out of seven animals operated on, there were two deaths. Animal "A" died on the tenth post-operative day. The animal was an old specimen and the animal house was extremely cold during the night before death. Post-mortem revealed no cause for death. The wound was healthy and there was no evidence of infection in the pleural cavity. Apart from some apical collapse, the lung was completely expanded. Exposure to cold appears to be the factor responsible for death. Great attention was paid to this aspect in all subsequent specimens.

Monkey "C" did not recover from the anaesthetic and died two hours after completion of operation. Post-mortem revealed that the left lung was completely fibrosed and practically non-existent. Dense pleural adhesions bound the lung down to the posterior chest wall. In view of the fact that the right lung is collapsed throughout the period of operation, the chests of the following animals were thoroughly examined before the operation was commenced.

/Re-operation

Re-operation was carried out at a varying period in each animal. The same procedure was adopted in anaesthetising the animal and in the preparation of the field of operation, as for the original operation. A plethysmographic record was, however, made of the normal as compared with the sympathectomised limb.

The original skin incision was visualised with great difficulty; the power of reparation is excellent in these animals. The scar was excised and the incision deepened through the fibrous tissue of the previous operation.

The lung was found to be adherent to the anterior chest wall in all cases. The adhesions were easily broken down by blunt dissection and the lung freed. The lung was also adherent posteriorly where the sympathetic chain had been removed. This, too, was gently and easily freed.

In "B" several strands of a pale, creamy material were found in the pleural cavity. It was removed completely and examined microscopically. No cells and no organisms were seen. Presumably it was fibrin clot.

In "B" and "D" the trachea and mediastinum were pulled over to the right side. The trachea was displaced in a curved manner and actually overlay the cut ends of the sympathetic trunk. The displacement was presumably partly due to collapse of the apex, and partly due to fibrosis at the site of pleural incision, pulling the mediastinal structures over.

The free caudal and cranial ends of the sympathetic trunk were readily visualised. The bed between was closely inspected for any semblance of an outgrowing fibre but none found. The stimulator was applied to both ends and the effect noted plethysmographically. Similarly, various areas in the posterior chest wall between the unconnected ends were stimulated and plethysmographic readings recorded.

Metallic clips were then inserted at the caudal and distal free ends of the sympathetic trunk to act as markers. The wound was again closed in layers and skin sutures inserted.

While the animals were still anaesthetised radiographs were taken to demonstrate the markers inserted.

Seven monkeys were sympathectomised, after the supply to the upper extremity had been ascertained by electronic stimulation. The following are the relevant features noted in each case.

MONKEY "A".

This animal was the oldest and the tamest of the series.

No difficulty was experienced with anaesthesia and the right chest was entered as described. In this case the apex of the lung was adherent and, on attempting to divide the adhesions, a cavity was entered. The cavity contained a thin, whitish, creamy material which was easily and completely removed. It seemed to be a loculated empyema cavity.

The sympathetic ganglia and trunk were readily seen. The pleura covering the posterior chest wall was incised and the sympathetic trunk defined by blunt dissection. The trunk was picked up on a blunt hook at various points and the stimulator applied direct to the nerve.

A positive response caused a drop in the total volume of the hand and a diminution of the pulse volume. The pulse

/and hand volumes

and hand volumes gradually returned to their previous levels. Working caudally from the stellate ganglion, where a strongly positive response was obtained, each sympathetic ganglion was stimulated in an attempt to determine the outflow of vasoconstrictor fibres to the upper limb. In this monkey stimulation of the ganglia from the stellate to the fourth thoracic ganglion resulted in vasoconstriction. (Figure 139. - page 356). Stimulation of the fifth thoracic ganglion was without any effect. (Figures 140. and 141. - pages 356 and 357).

Thus the sympathetic outflow to the upper extremity was confined to the sympathetic trunk from the fourth thoracic ganglion to the stellate.

No evidence of vasodilatation was noted as a result of stimulation.

The sympathetic trunk was divided at the lower border of the fourth rib and dissected, cranially, to a point just below the stellate ganglion. The ganglia, chain and all connecting rami were cut and removed. The cut caudal end was stimulated once again to determine the completeness of the sympathectomy - no vasoconstriction resulted.

This specimen took some eighteen hours to recover fully from anaesthesia but then resumed a normal routine. On the ninth day, however, following a bitterly cold night, the animal was found pulseless, cold and comatose. It was revived with intravenous coramine and warmth and took some food of its own accord. Special precautions were taken but, owing to an electrical fault, the heating apparatus failed during another cold night. The animal succumbed on the tenth post-operative day.

Post-mortem revealed a wound firmly healing. There was some collapse of the right apex but no apparent cause for death could be found.

The sympathetic chain was found exactly as left at operation. (Figure 142. - page 358).

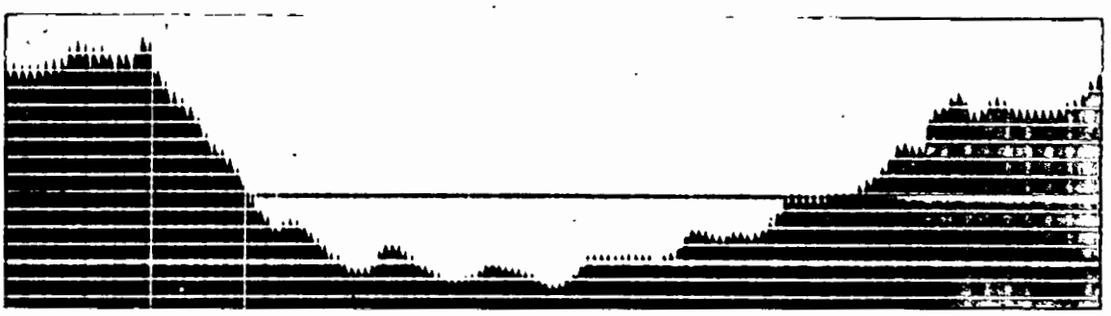


FIGURE 139. - "A"

Stimulation of the fourth thoracic ganglion.

(White lines indicate duration of the stimulus).

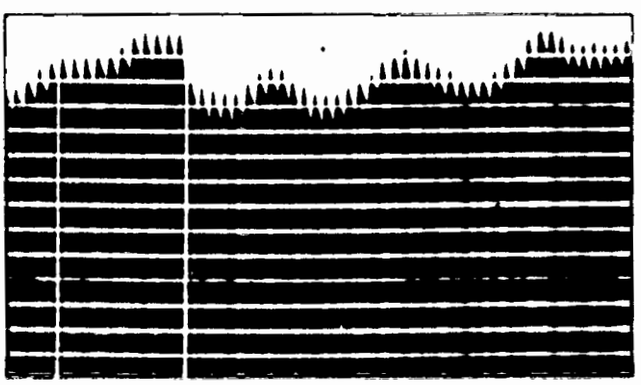


FIGURE 140. - "A"

Stimulation of the fifth thoracic ganglion.

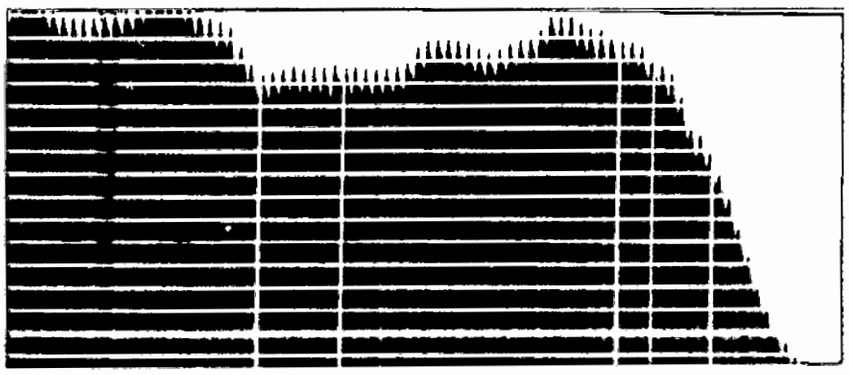


FIGURE 141. - "A"

Stimulation of the fifth thoracic ganglion and the fourth thoracic ganglion.

FIGURE 142. - "A"

Post-mortem findings on the tenth post-operative day.

"B"

This specimen was the only one to have any vessel lying anterior to the sympathetic trunk. The fourth intercostal vein crossed the sympathetic trunk anteriorly to enter the azygos vein. The remaining intercostal vessels all lay posterior to the trunk.

The fourth intercostal vein proved a useful localiser in stimulation. It was found that stimulation of all points caudal to the vein produced no effect on the plethysmograph, whereas all points cranially resulted in vasoconstriction. (Figure 143. - page 362). No evidence of vasodilatation was noted on stimulation of the sympathetic chain and ganglia before sympathectomy.

The chain was divided at the site of this intercostal vein, which was inadvertently injured. The vein was thus divided, and both ends ligated. The resection of the chain was carried cranially to a point just below the stellate ganglion.

The bed of the sympathetic was stimulated between the cut ends to check completeness of the operation. No vasoconstriction resulted. (Figures 144. and 145. - pages 362 and 363).

Stimulation of the lower end of the stellate ganglion resulted in a momentary rise in the hand volume lasting four seconds followed by vasoconstriction and a fall in the hand volume. (Figure 146. - page 363).

On examining the piece of tissue removed, it was found that a small piece of the stellate ganglion was incorporated in the section. This was confirmed by the presence of a Horner's Syndrome, observed when the animal was seen next day.

/The animal

The animal was observed at regular intervals after operation and, although skin temperature recordings were not obtained, the right hand (sympathectomised) was observed to be always warmer than the left (non-sympathectomised). Also the Horner's Syndrome was present throughout. Eighteen months after the original operation, miosis, drooping of the upper lid, and narrowing of the palpebral fissure were still present.

112 days after original operation, the animal was again anaesthetised and the thorax opened through the original incision. Before any operative manoeuvre was performed, plethysmographs were taken of both the non-sympathectomised and the sympathectomised hands. (Figure 147. - page 364). A marked difference is seen in the relative pulse volumes. In comparison with a plethysmograph of the right hand before sympathectomy under the same conditions of anaesthesia, there is no doubt which is the sympathectomised limb. (Figure 148. - page 364). The pulse volume of the sympathectomised hand before sympathectomy was 0.02cc., and after sympathectomy it was 0.01cc. Under identical conditions the pulse volume of the non-sympathectomised limb was 0.02cc.

On opening the thorax, the lung was found to be adherent to the anterior chest wall. These adhesions were divided by blunt dissection. Much "fibrin clot" was found and removed. The apex of the lung was collapsed. The trachea and superior mediastinum were deviated over to the right side. The tracheal deviation was a gentle curve convex to the right.

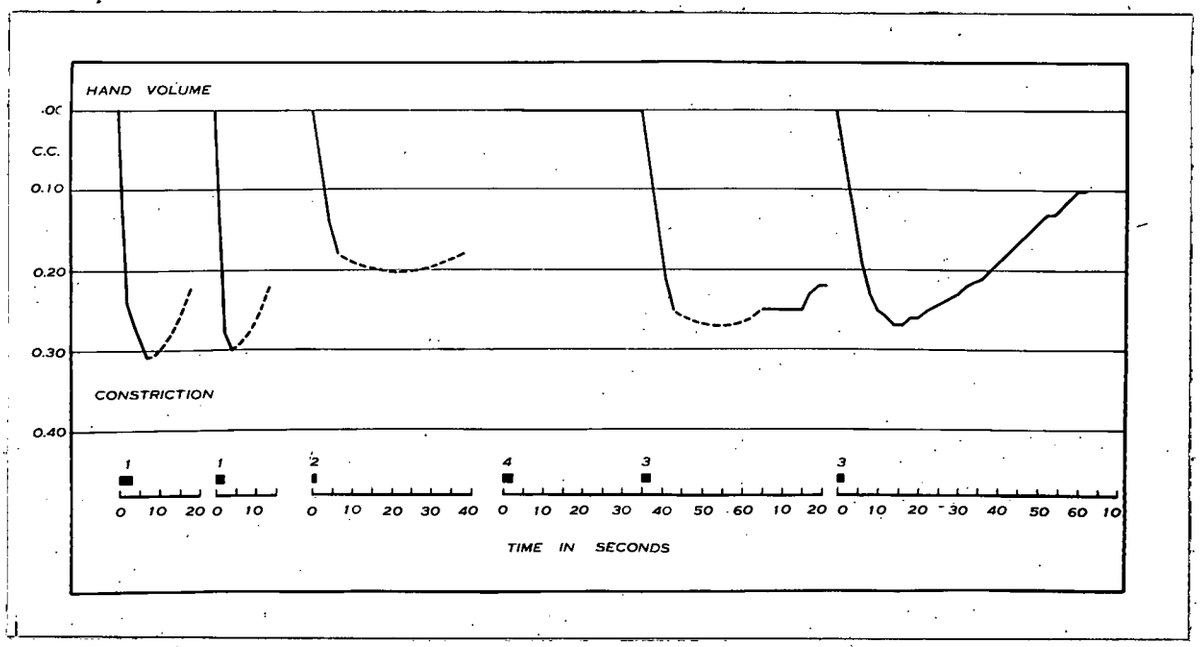
The lung was also adherent posteriorly, at the site of the pleural incision. These adhesions also were removed by blunt dissection. The anaesthetist found that,

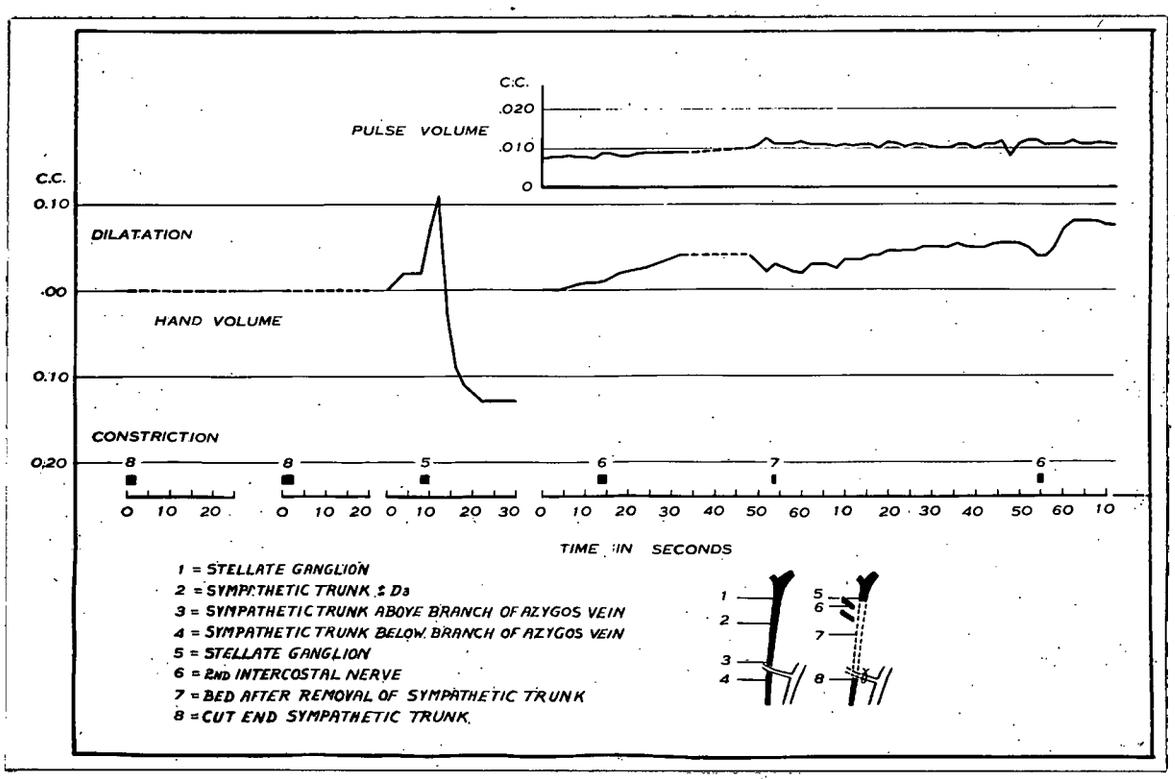
/after the posterior

after the posterior adhesions had been divided, it was possible to inflate the whole lung completely.

No evidence of communicating fibres between the two cut ends of the sympathetic chain was found. The stimulator was applied at the caudal end. No response was elicited.

There was thus no evidence of vasoconstrictor fibres between the cut ends of the sympathetic chain 112 days after sympathectomy.





FIGURES 143. and 144. - "B"

Graphic representation of
stimulation of the sympathetic ganglia at operation.

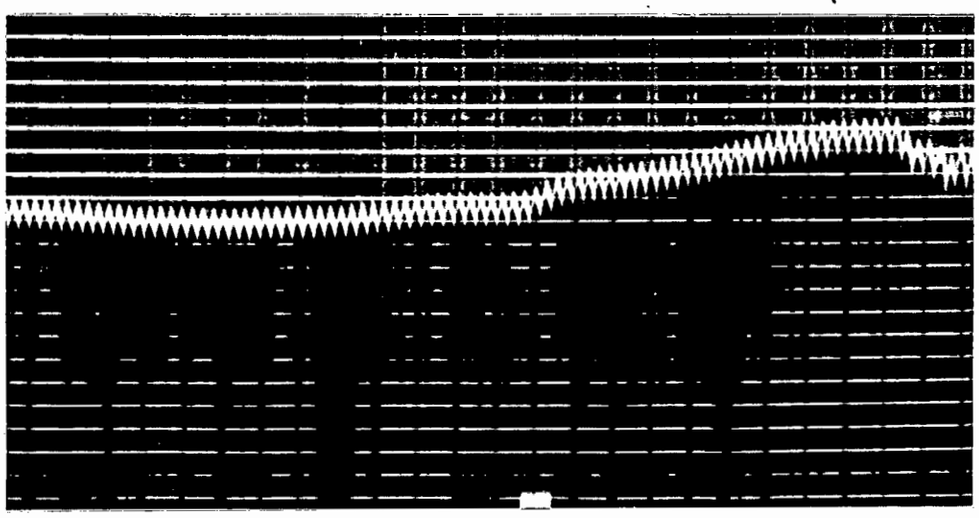


FIGURE 145. - "B"

Stimulation of the bed of the second thoracic ganglion after sympathectomy.

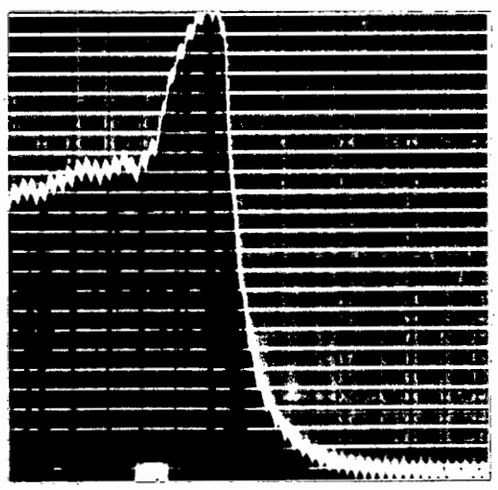


FIGURE 146. - "B"

Stimulation of stellate ganglion after sympathectomy.

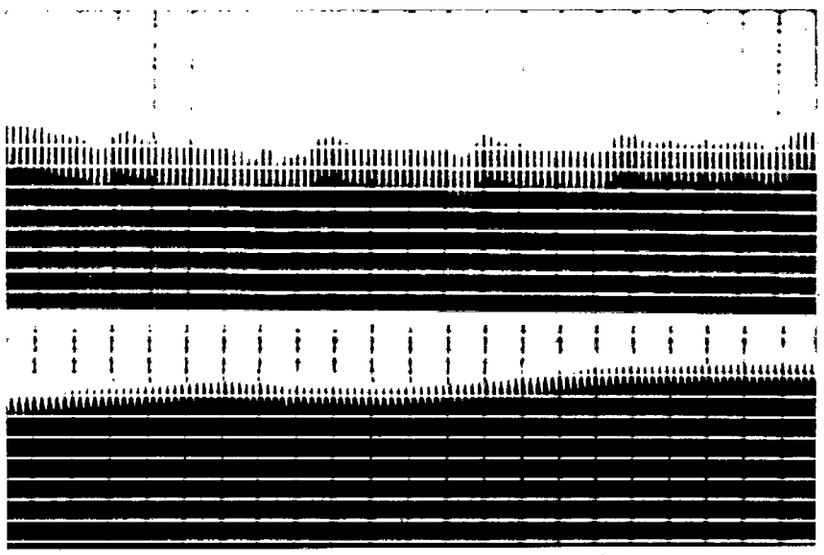


FIGURE 147. - "B"

Left hand (upper tracing) and right hand.

Right hand sympathectomised by removal of Th.2, Th.3 and Th.4 112 days previously.

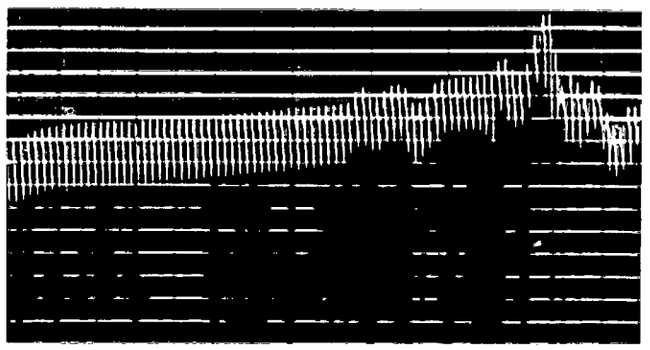


FIGURE 148. - "B"

Right hand under anaesthesia before sympathectomy.

"C"

There was no difference in the procedure adopted with this animal.

After the sympathetic chain had been exposed, stimulation produced vasoconstriction from the stellate as far caudally as the sixth thoracic ganglion. Thus stimulation of the second, fourth, fifth and sixth thoracic ganglia all resulted in vasoconstriction. (Figures 149. and 150. - page 366). Stimulation of the third thoracic ganglion did not have any vasoconstrictor effect. (Figure 151. - page 367). Stimulation of the trunk below the sixth ganglion was also without effect.

After division below the sixth ganglion, the trunk was stimulated. Caudal to the section no vasoconstriction resulted, whilst cranial to the section vasoconstriction was elicited. (Figure 152. - page 367). After dividing all the rami communicantes from the second to the sixth thoracic ganglia, the trunk and intervening section was removed.

This animal did not recover consciousness after the anaesthetic and died two hours later. Post-mortem examination revealed a fibrosed, functionless left lung.

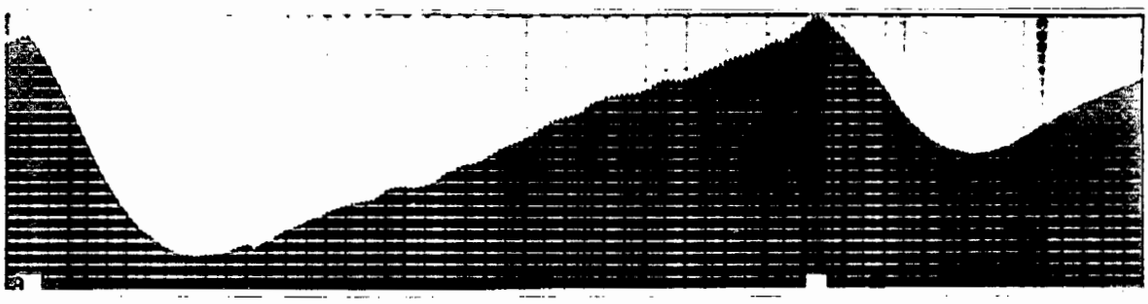


FIGURE 149. - "C"

Stimulation of the fourth and fifth thoracic ganglia.

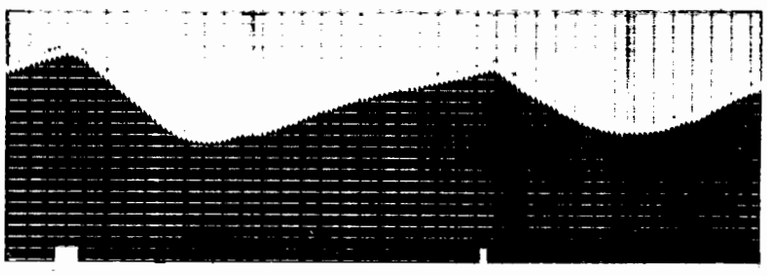


FIGURE 150. - "C"

Stimulation of the sixth thoracic ganglion on two occasions. Note the difference in response to the shorter stimulus.

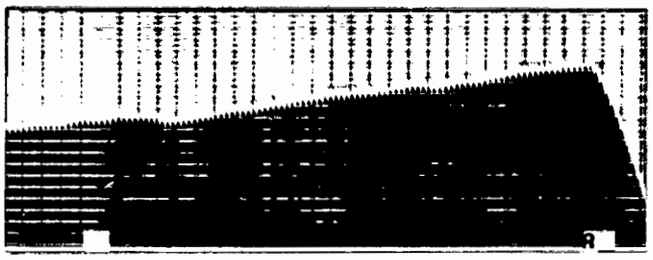


FIGURE 151. - "C"

Stimulation of the third thoracic ganglion and the fourth thoracic ganglion.

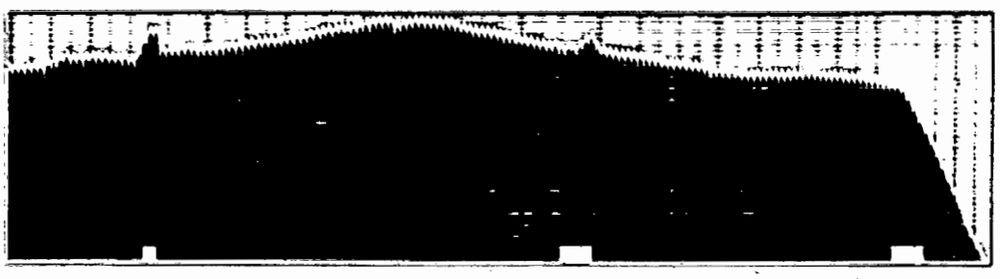


FIGURE 152. - "C"

Stimulation of the seventh thoracic ganglion twice and the sixth thoracic ganglion after division of the chain below the sixth thoracic ganglion.

"D"

There were no unusual features in the anatomy of the sympathetic chain and ganglia in this specimen.

Vasoconstriction resulted from stimulation of the stellate ganglion and the ganglia situated in the second, third and fourth spaces. The second, third and fourth thoracic ganglia were, therefore, removed.

Immediately post-operatively the right (sympathectomised) hand was warmer than the left. There was no evidence of a Horner's Syndrome.

Repeated observation subsequent to operation confirmed the warmth of the right hand as compared with that of the non-sympathectomised left hand.

98 days after the original operation, the thorax was re-opened under anaesthesia. Skin temperatures of the hands were taken before anaesthesia was begun:-

Palm of right hand ... 28.3°C.
Palm of left hand ... 25.2°C.

There was thus a difference of 3.1°C. between the sympathectomised and the non-sympathectomised limbs.

Under full surgical anaesthesia, the temperature of the non-sympathectomised left hand rose to 34.2°C., whilst the skin temperature of the sympathectomised right hand dropped to 27.8°C.

Plethysmographic records of both the sympathectomised and non-sympathectomised hands again revealed a marked difference. (Figure 153. - page 370). The pulse volume of the non-sympathectomised hand is 0.008cc. and the sympathectomised limb 0.003cc., both under full surgical anaesthesia.

/The pulse volume

The pulse volume of the sympathectomised limb under anaesthesia previous to operation was 0.015cc. (Figure 154. - page 370).

Before the thorax was re-opened through the original incision, it was noted that the apex beat was displaced to the right side. On opening the thorax the lung was adherent to the anterior chest wall and to the posterior chest wall. The sympathetic stump was defined, no macroscopic evidence of continuity being found.

Silver clips were inserted at the free cut ends of the sympathetic trunk. The animal was then radiographed.

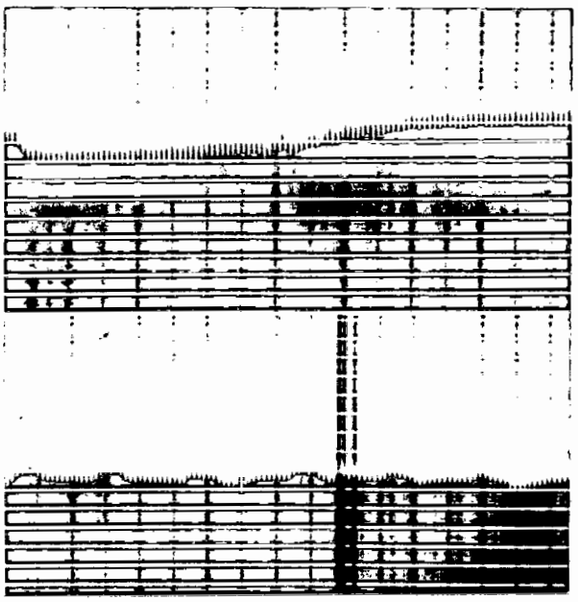


FIGURE 153. - "D"

Left hand (upper tracing) and right hand under anaesthesia.

Right hand sympathectomised by removal of Th.2, Th.3 and Th.4 98 days previously.

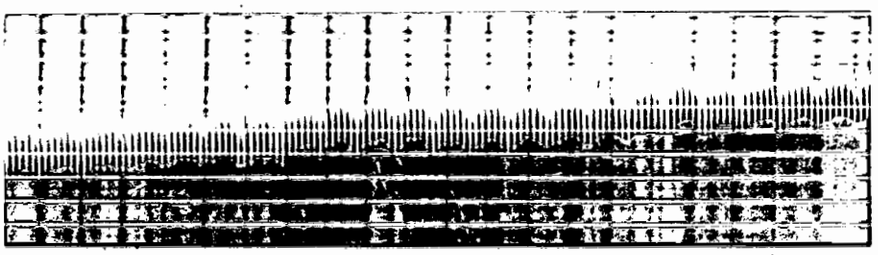


FIGURE 154. - "D"

Right hand under anaesthesia before sympathectomy.

"E"

There was no anatomical departure from the ordinary in this specimen. On entering the thorax the sympathetic chain could be seen shining through the pleura covering the posterior chest wall. The sympathetic chain was stimulated through the parietal pleura. A small fall in hand volume occurred after an apparent initial rise. (Figure 155. - page 373).

After the pleura had been incised, the sympathetic trunk itself was stimulated at the same point, i.e. the second thoracic ganglion. A definite fall in the hand volume and pulse volume was seen. (Figure 156. - page 373). Vasoconstriction was obtained on stimulating the stellate, second, third and fourth thoracic ganglia. The rami of the second, third and fourth thoracic ganglia were divided and the trunk was cut just below the fourth thoracic ganglion and just below the stellate ganglion. After the sympathetic trunk had been divided between the stellate and second thoracic ganglia, the caudal end was stimulated. No vasoconstriction resulted. (Figure 157. - page 374).

Stimulation of the bed had no vasoconstrictor effect. (Figure 158. - page 374). The sympathectomy appeared complete.

Next day the sympathectomised limb was warmer than the non-sympathectomised. It has remained warmer ever since.

No Horner's Syndrome resulted.

106 days after sympathectomy the animal was anaesthetised for re-operation. Prior to operation, plethysmographs were taken of the sympathectomised and non-sympathectomised hands. A marked difference is seen on the two sides. The pulse volume of the non-sympathectomised hand is 0.013cc.,

/whereas

whereas that of the sympathectomised hand is 0.006cc. (Figure 159. - page 375). The pre-sympathectomy pulse volume of the sympathectomised hand is 0.018cc. (Figure 160. - page 376).

The incision was found to be soundly healed. Several deep chromic sutures were partly absorbed. The lung was adherent both to the anterior and posterior chest wall. The apex of the lung was collapsed and could not be completely aerated under positive pressure.

The divided ends of the sympathetic chain were easily identified. There was no macroscopic evidence of continuity. The caudal end was stimulated. No vasoconstrictor effect was noted. Although no fibres were seen connecting the two ends of the sympathetic chain, the whole bed was stimulated in an attempt to determine whether any sympathetic fibres had re-established continuity. No evidence of continuity was obtained.

Thus, at 106 days, there was no evidence indicative of return of vasomotor tone to the vessels of the upper limb.

Silver clips were inserted at the free ends of the sympathetic trunk to act as markers. The animal was X-rayed after the chest wall had been sutured in layers.

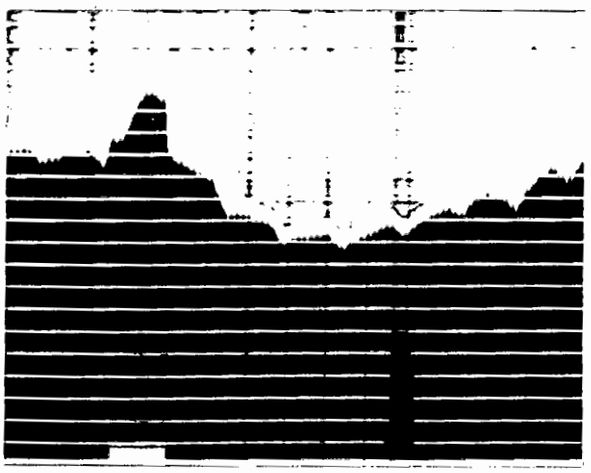


FIGURE 155. - "E"

Stimulation of the second thoracic ganglion through the intact overlying pleura

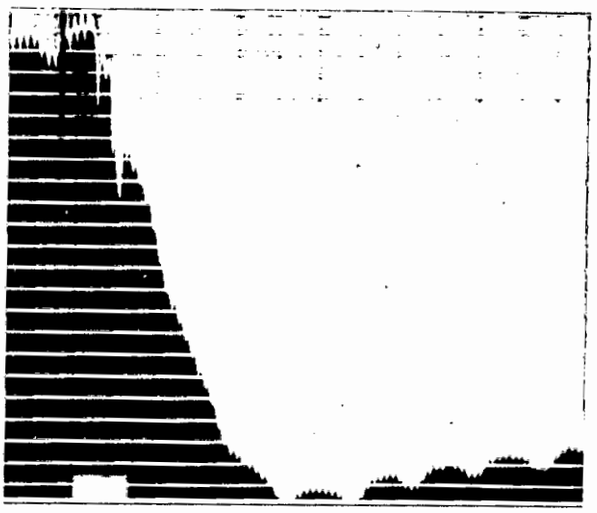


FIGURE 156. - "E"

Stimulation of the second thoracic ganglion direct - after the overlying pleura had been incised.

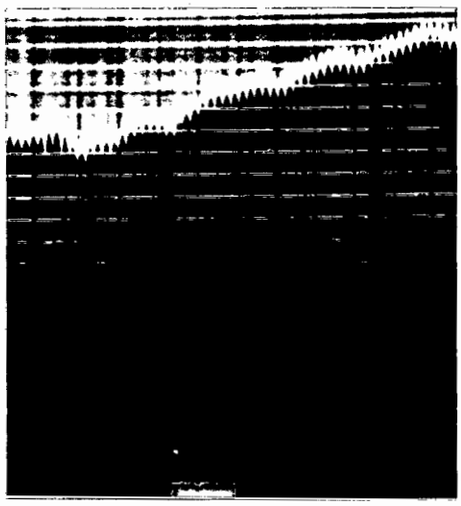


FIGURE 157. - "E"

Stimulation of the second thoracic ganglion after division of the trunk between the stellate and second ganglia.

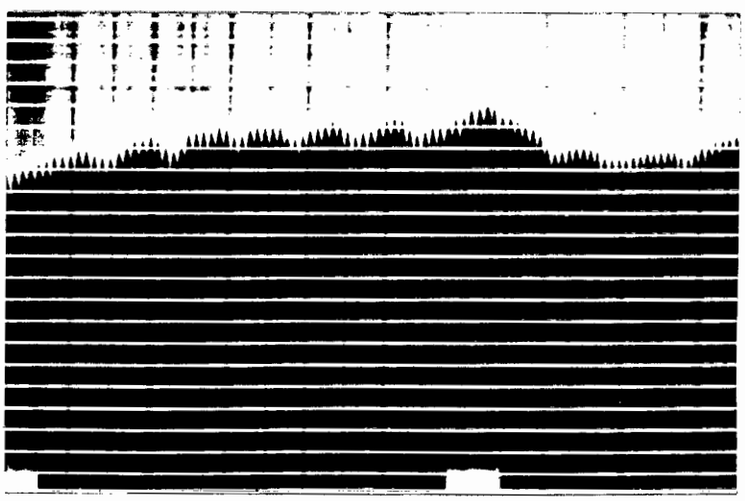


FIGURE 158. - "E"

Stimulation of the bed of the sympathetic after sympathectomy.

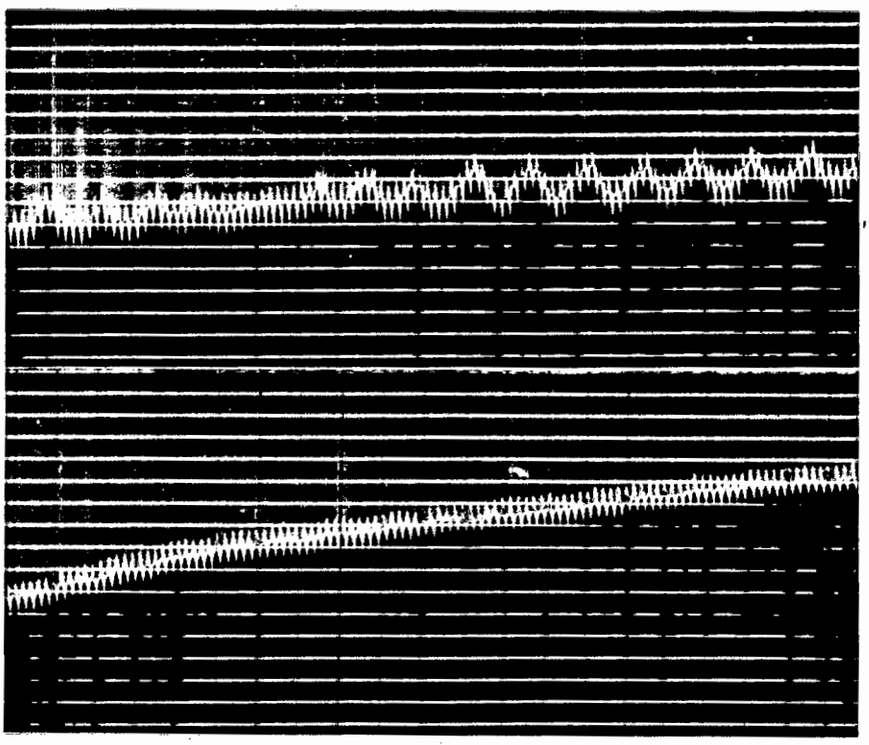


FIGURE 159. - "E"

The left hand (upper tracing) and the right hand under anaesthesia.

Removal of right Th.2, Th.3 and Th.4 106 days previously.

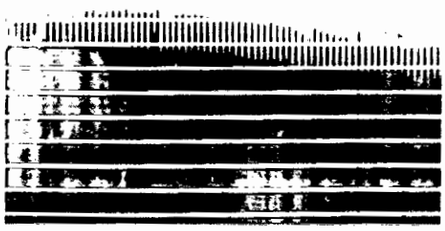


FIGURE 160. - "E"

Right hand under anaesthesia before sympathectomy.

"F"

It was decided to remove the stellate ganglion in this monkey. The incision, thus, was centred over the second space, in the belief that the approach to the stellate ganglion would be easier. The second rib was removed and the cartilage of the first rib divided. The stellate ganglion was easily seen.

Stimulation of the various ganglia determined that the third and second thoracic ganglia and the stellate ganglion only contained fibres to the upper limb. The trunk was divided just below the third thoracic ganglion and the rami communicantes to the second and third intercostal nerves were cut. The stellate ganglion was pulled down and all its rami divided. The two loops, around the subclavian artery, were divided close to the stellate ganglion. The stellate, second and third thoracic ganglia were thus excised. Stimulation of the sympathetic bed failed to produce any vasoconstrictor response thereafter.

The sympathectomised hand was warmer next day and has persistently remained so.

As expected, a Horner's Syndrome resulted. It has persisted and is still present eighteen months after operation.

105 days after initial operation the animal was prepared for re-operation. Before anaesthesia, skin temperature recordings revealed no difference in the sympathectomised and non-sympathectomised sides - 26.5°C.

After anaesthesia, however, the sympathectomised hand recorded 27.5°C., whilst the skin temperature of the non-sympathectomised hand read 34.2°C.

/On entering

On entering the thoracic cavity, through the soundly healed original incision, the lung was again adherent both to the anterior and posterior chest wall. Although there was slight tracheal deviation to the operated side, the displacement was not as gross as in the other specimens.

The sympathetic chain was visualised running up to the third space where it had been sectioned previously. Above this level there was no evidence of sympathetic trunk or ganglia. The upper sympathetic (actually cervical) could not be demonstrated from this approach.

The distal end was stimulated and no effect was observed on the plethysmograph. Stimulation was applied to several areas of the sympathetic bed without any evidence of activity.

Stimulation of the first thoracic nerve resulted in muscular contraction only.

Thus, 105 days following removal of the stellate and second and third thoracic ganglia, no evidence of sympathetic activity was present in the upper limb.

In an attempt to note whether any vasoconstrictor fibres were present in the phrenic nerve, stimulation was applied. Convulsive movements of the diaphragm resulted but no effect was observed on the pulse or hand volume.

Similarly, vagal stimulation had no effect on the pulse or hand volume of the sympathectomised limb.

/"G" The same

"G"

The same procedure was adopted with this animal as with "F", i.e. the stellate ganglion plus the ganglia responding to stimulation were to be removed.

It had previously been noted that there was a difference in the pulse volume of the limb to be sympathectomised, before and after the pleural cavity had been entered, i.e. the presence of a pneumothorax diminished the amplitude of the pulse. Tracings were, therefore, taken under the same conditions of anaesthesia before, and after, thoracotomy.

The pulse volume under anaesthesia before thoracotomy was 0.005cc. (Figure 161. - page 383) and, after, 0.002cc. Also respiratory waves were more noticeable on the recording taken after opening the pleural cavity. (Figure 162. - page 383)

Stimulation of the sympathetic trunk revealed that the outflow to the upper limb was through the second and third thoracic and the stellate ganglia. Accordingly, all the rami of the second and third thoracic ganglia were cut and the trunk sectioned below the third thoracic ganglion. The rami of the stellate ganglion were then defined, sectioned, and the sympathetic trunk and ganglia removed.

Stimulation of the stellate ganglion, in addition to the vasoconstrictor effects of the hand, also produced a dilatation of the pupil. This dilatation was not seen if the stimulator was applied caudal to the stellate ganglion.

Stimulation of the bed after sympathectomy had no effect on the volume of the limb. Sympathectomy appeared complete. Stimulation of the vagus also had no effect on the limb.

/Observation

Observation next day revealed a Horner's Syndrome, which was unchanged 98 days after operation.

The sympathectomised limb is still warmer than the non-sympathectomised.

84 days after sympathectomy "G" was re-operated on. The second rib only had been removed in this specimen. After induction with sodium pentothal intravenously, plethysmographs were taken of both the sympathectomised and non-sympathectomised hands. Again it is noted that the pulse volume of the non-sympathectomised limb is greater than the sympathectomised. (Figures 163. and 164. - page 384).

On entering the thoracic cavity through the original incision, the lung was found to be adherent to the anterior chest wall. A small area of collapse of the upper lobe was noted. The lung was adherent wherever the parietal pleura had been interrupted. The non-vascular adhesions were separated by blunt dissection and the lung completely freed.

The cut end of the sympathetic chain was identified just above the fourth rib. Radiating up towards where the stellate ganglion originally was, were two fibrous strands. Application of the stimulator to these bands had no effect on the pulse or hand volume. Thus there was no evidence of sympathetic nerve fibres in these strands.

The bed of the sympathetic chain was stimulated atvarious points. No evidence of vasoconstrictor or vasodilator fibres was found.

No sign of any of the rami of the stellate ganglion was seen. Dissection in the region of the subclavian artery failed to reveal any sign of the two loops around the artery. Stimulation of this area again was without effect on the pulse.

/The vagus

The vagus was defined and stimulated. Stimulation was without effect either on the pulse volume or the heart rate.

In order to define the sympathetic trunk cephaled to the ablated stellate ganglion, it was decided to approach the structures via the neck. Accordingly, through the same incision, the medial end of the clavicle was disarticulated at the sterno-clavicular joint. Some of the sternal fibres of the sterno-mastoid were divided and the freed clavicle displaced upwards and laterally. The scalenus anterior was divided close to its insertion into the first rib and the subclavian vessels exposed. The carotid sheath was then opened and each structure defined.

The internal jugular vein was lateral to the carotid artery, and lateral and posterior to the vein lay a single nerve trunk. No other trunk or chain was visible at this site. This nerve was continuous with the vagus in the thorax. It was thought that, in view of the absence of a definite cervical sympathetic chain, the sympathetic and vagus together constituted a single vago-sympathetic trunk.

This single trunk was, therefore, stimulated and the effect on the pupil noted. Dilatation ensued; this confirmed the presence of sympathetic fibres within the single trunk.

At the same time, plethysmographic records showed no sign of vasoconstriction. No vasoconstrictor or vasodilator effects were observed on stimulation of the vago-sympathetic trunk at any point along the course. Yet, each time, dilatation of the pupil ensued.

A silver clip was placed on the vago-sympathetic trunk. The clavicle was restored to the sternum and fixed there by sutures through the periosteum of both bones. All

/the divided

the divided muscles were then sutured in position.

Silver clips were inserted at:- (1) the free cut end of the thoracic sympathetic chain, and (2) the site judged to have been the site of the lower pole of the stellate ganglion. The thoracic wound was then sutured in layers and the skin incision closed.

The animal was then X-rayed and the position of the clips noted.

In spite of the extensive manipulation, the animal recovered full consciousness within three hours of completion of the operation.

Sympathectomy of the upper extremity still appears to be complete 84 days after section of the stellate and second and third thoracic ganglia.

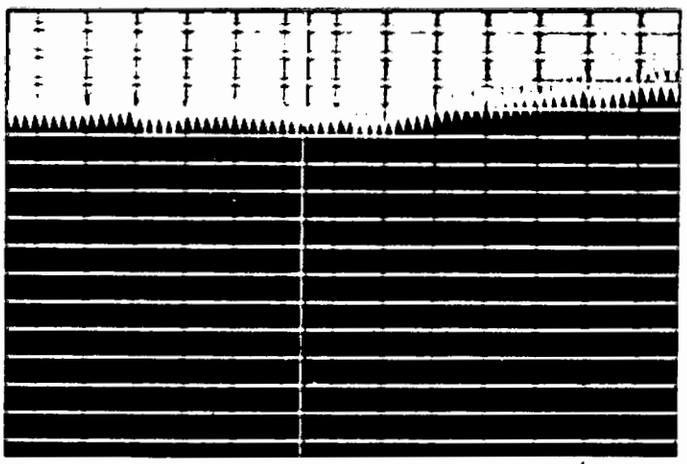


FIGURE 161. - "G"

Right hand under anaesthesia before thoracotomy.

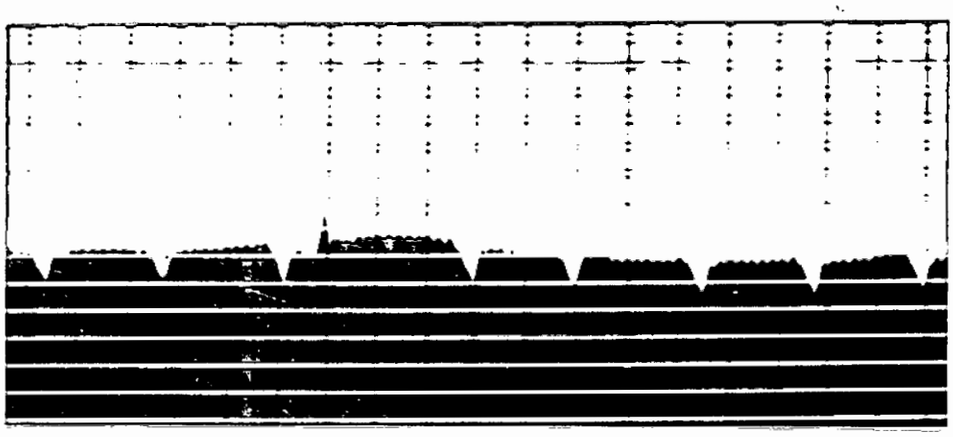


FIGURE 162. - "G"

Right hand under anaesthesia after thoracotomy.

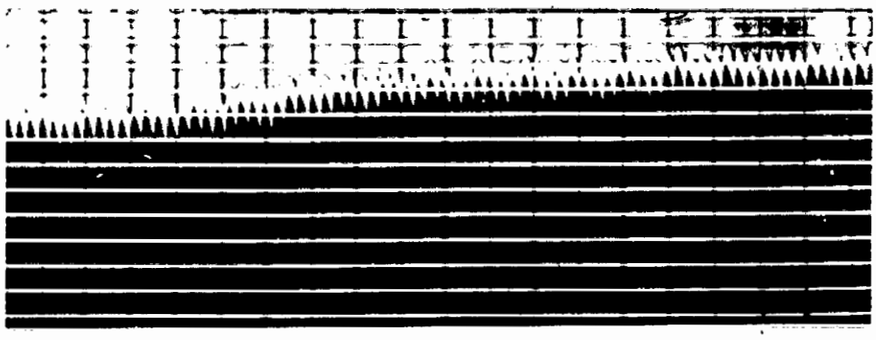


FIGURE 163. - "G"

Left hand (non-sympathectomised) under anaesthesia.

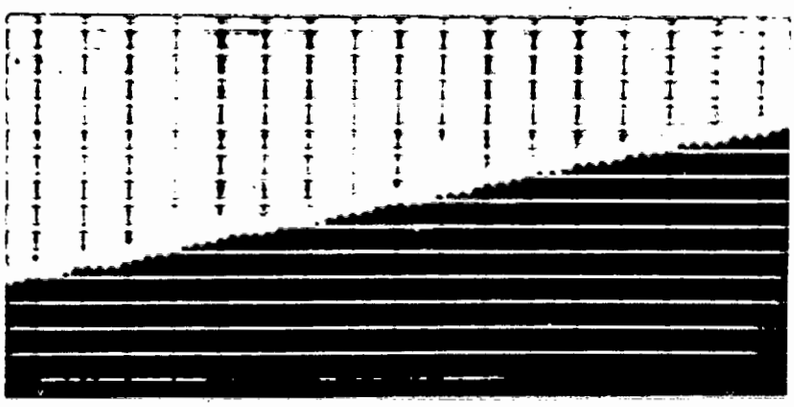


FIGURE 164. - "G"

Right hand-under anaesthesia.

Right stellate, second and third thoracic ganglia removed 84 days previously.

(c) HISTOLOGY.

The right second, third and fourth thoracic ganglia, together with the intervening sympathetic chain, were removed in "B". The animal died eighteen months after sympathectomy. Post-mortem examination failed to reveal any definite cause of death. The mediastinal structures were deviated to the right - this feature had been noticed at re-operation twelve months previously. The lung was adherent to the pleura anteriorly. The apex of the lung was collapsed and, posteriorly, the lung was adherent to the thoracic wall. A plane of cleavage was readily demonstrable and the adherent lung was easily separated both anteriorly and posteriorly.

Inspection of the posterior wall of the right thorax was undertaken with the thoracic viscera in situ. The stellate ganglion was visualised at the apex of the pleura but the chain ended abruptly just below the lower border of the first rib. No sympathetic chain, i.e. trunk or ganglia, was visible over the second, third, or fourth ribs or in the corresponding rib spaces. The sympathetic chain was easily identified on the neck of the fifth rib and caudally therefrom was continuous to the diaphragm.

The macroscopic findings are represented diagrammatically in Figure 165. (page 393).

In view of the absence of any obvious macroscopic communication between the upper and lower free ends of the sympathetic chain, microscopic examination of the denervated area had to be undertaken.

Therefore, the thoracic viscera were removed. The head and upper cervical structures were amputated through the fourth cervical disc and the lower part of the body was severed

/through the upper

through the upper border of the eighth thoracic vertebra. Thus a block of tissue was left, extending from the fifth cervical vertebra cranially to the seventh thoracic vertebra caudally. Both the sympathectomised right and the normally innervated left sides were included in the block. Laterally, the block extended to one-and-a-half inches from the midline. This ensured that any sympathetic nerve or fibre would be included in all sections cut.

The block of tissue was placed in acid, en masse, for decalcification. After several days the block was divided into right and left halves by longitudinal section through the middle of the vertebral bodies. This ensured that any section would not be too large and would include all the essential structures of one side. Each half could be identified easily and there was no likelihood of error.

After further decalcification the right half was divided into nine equal parts of tissue, each of which was prepared in blocks for paraffin section, to retain every bit of tissue on this, the operated, side. Horizontal sections of each paraffin block were cut. Each section, therefore, consisted of the right half of the body of the vertebra and spinal cord, the costo-vertebral junction and one to one-and-a-half inches of the corresponding rib. On the anterior surface of the rib and vertebra were the retro-pleural tissues. The paravertebral muscles could be identified on the posterior aspect.

Several blocks were made of the normal left side at various heights. These blocks acted as controls. (Figures 166. and 167. - pages 394 and 395).

Sections, 10μ in thickness, were cut off every block. Each section was retained and the block could be examined serially. A few sections of each block were stained

/with haematoxalin

with haematoxalin and eosin. This method of staining sufficed for ordinary examination. Where, however, doubt existed about the nature of tissue or fibre, appropriate stains were used to demonstrate either nerve or connective tissue fibres.

Great difficulty was encountered in finding a suitable stain for nerve fibre or other nerve tissue. However, after many trials and as many errors, Romanes' (1946) modification of the silver nitrate stain proved most satisfactory. Even with this stain, it was only an accidental alteration of temperature that produced results.

For connective tissue or other tissue containing collagen, Azan's stain proved the best.

At the level of the eighth cervical disc, the stellate ganglion was observed lying just anterior to the costo-vertebral articulation. In the first few sections the ganglion appeared as two separate masses. This was due to the section cutting the ganglion at its concavity. As the ganglion was traced down, however, it became one rounded trunk. There was a fine perineural layer of connective tissue, surrounding the ganglionic mass. No reaction in the surrounding areolar tissue could be observed.

The sympathetic trunk, as observed, was continued throughout the block of tissue to the lower border of the first thoracic vertebra. However, as the last few sections (A in Figure 165.); were cut, it was noticeable that the ganglionic mass was less in amount and the perineural sheath was thicker than previously. In the areolar tissue immediately surrounding the sympathetic trunk, cellular masses were apparent on the posterior and antero-medial aspects. That mass on the antero-medial aspect had a reticular, slightly whorled appearance.

/(Figure 168.

(Figure 168. - page 396). Numerous thin-walled capillaries were present nearby. There was no apparent connection between the reticular whorled mass and the trunk itself. In the last section taken from this block, the sympathetic trunk was still present although much reduced in size. The surrounding tissue was slightly bigger but had essentially the same appearance.

The upper border of the following block was through the inter-vertebral disc between the first and second thoracic vertebra. (B in Figure 165.). In the first section taken from this block, the sympathetic trunk was not present. No ganglion cells were demonstrable at this site. Anterior to the costo-vertebral angle, i.e. corresponding to the expected site of the sympathetic trunk, was a mass of tissue closely resembling the structures observed in the previous block. The mass of tissue was roughly triangular in shape. (Figure 169. - page 397). It was not well defined and tapered off anteriorly. There was no surrounding fibrous capsule. The mass was very cellular and had a reticulated, whorled appearance. Numerous capillaries were scattered throughout the tissue.

Higher magnification (Figure 170. - page 398) confirms the whorled appearance. The mass consists essentially of fibrous tissue. Scattered throughout this fibrous tissue, however, are many small fibres, seen as small pyknotic centres surrounded by a clear zone and surrounding this is a thin membrane-like structure.

The Azan stain confirmed the large amount of fibrous tissue present in the section. The centre part of the small fibres, however, did not take up the collagen stain. By using the Romanes' modification, these fibres were shown to take up the silver nitrate stain. It is likely, therefore,

/that these structures

that these structures respresent small nerve fibres. Other nerves in the section have the same appearance when this stain is used.

Further sections of this block continued to show the cellular fibrous mass at the same anatomical site. The mass retains its triangular shape. (Figure 171 - page 399). The tissue, however, appears denser and even more cellular. The same type of fibre is present. In one concentrated area the appearance was very much like that of a rosette. In the lowermost pole of the mass a single fibre is seen out longitudinally. This is seen at a higher magnification in Figure 172. (page 400). The fibre, apparently unconnected with any other structure, is seen as a single deeply staining "thread" surrounded by a sheath. (Figure 173. - page 401). Romanes' nerve stain confirmed the nature of this fibre, which apparently is a myelinated nerve fibre. Diligent search of the cellular mass failed to reveal another such fibre.

The areolar cellular infiltration was more intense in this section than in the previous sections. It was almost completely round cell in type.

Still further caudally, at the lower border of the second rib, the mass of fibrous tissue, was still present. It was considerably smaller in amount, although the same general outline was retained. (Figure 174. - page 402). Higher magnification of the same section showed the fibrous tissue to be denser. The fibres were fewer in number but more easily defined. They seemed to be dispersed over a slightly wider area and not arranged in bundles, as previously noted. (Figure 175. - page 403). No nerve fibres appeared to be sectioned longitudinally in this section.

/Sections taken

Sections taken at the lower border of the second thoracic vertebra, showed that the fibrous and cellular mass was considerably smaller in size than at the upper border. A few nerve fibres could be seen just anterior to the intercostal nerve.

At the upper border of the third thoracic vertebra, no evidence of the cellular mass was found. Diligent search failed to reveal any sign of a nerve fibre or excessive connective tissue.

At the upper border of the fourth rib, at the lower border of the third thoracic vertebra, slightly medial to the costo-vertebral articulation four or five fibres were seen. (Figure 176. - page 404). The fibres were surrounded by fairly dense fibrous tissue. There was no definite shape to this aggregation. Nearby were several small capillaries and a larger vessel lay slightly more laterally. A round cell infiltration was present in the surrounding areolar tissue. These features are well shown in the higher magnification. (Figure 177. - page 405).

Numerous small fibres were demonstrated at the upper border of the fourth thoracic vertebra. The fibres were not surrounded, however, by the same amount of fibrous tissue as in the other sections, (Figures 178. and 179. - pages 406 and 407), but rather by a cellular oval-shaped tissue.

Slightly caudally, ganglion cells again appeared. These cells were embedded in an oval-shaped mass of fibrous tissue, without any definite perineural sheath. The ganglion cells did not differ from ganglion cells observed in other parts of the sympathetic nervous system. They were less numerous and arranged in an oval instead of a spherical

/manner.

manner. (Figures 180. and 181. - pages 408 and 409).

Traced caudally from this level, the sympathetic trunk rapidly assumed the appearance of normal sympathetic tissue, as on the normal opposite side.

At the level of the sixth thoracic vertebra a section shows the spinal nerve emerging from the intervertebral foramen. (Figure 182. - page 410). Included in the spinal nerve is a part of the posterior root ganglion. Anterior and medial to the nerve lies the sympathetic trunk, actually represented by a ganglion. A ramus is either entering or leaving the ganglion.

Summary:

Sympathectomy in this monkey had been performed by removal of the second, third and fourth thoracic ganglia. All sympathetic tissue from the first intercostal space, just below the lower border of the first rib, to the fourth intercostal space just below the lower border of the fourth rib, has been removed. At this lower pole, the sympathetic trunk had been crossed anteriorly by the fourth intercostal vein.

Four months after operation there was no macroscopic evidence of communication between the two ends. Electronic stimulation could not determine any return of function, and plethysmographic studies under anaesthesia indicated that there had not been a return of vasomotor tone.

Eighteen months after operation, on the death of the animal, there was no macroscopic continuity between the severed ends of the sympathetic.

Microscopically, it was possible to demonstrate that the lower pole of the stellate ganglion was continued as a mass of fibrous tissue together with numerous myelinated fibres. Traced caudally these structures were present as far as the

/upper border

upper border of the third rib. At this point there was neither this fibrous tissue and nerve fibre mass, nor was there any evidence of a normal sympathetic chain.

At the upper border of the fourth rib a few fibres of the same tissue reappeared and could be followed to the upper border of the fifth rib.

Apart from the complete absence of any structures at the level of the third rib, a few fibres were visible below at the upper border of the fourth rib.

Traced caudally, therefore, the sympathetic trunk ends abruptly surrounded by a fibro-cellular tissue which is continued caudally in diminishing amount as far as the third rib. At this point there is no evidence of either sympathetic chain or nerve fibres.

Caudal to the third rib, some few fibres are present at the fourth rib, gradually increasing in number as traced distally, finally being replaced by ganglion cells. Still further caudally the sympathetic trunk assumes its normal characteristics.

Conclusions:

There has been a down-growth of myelinated nerves from the lower pole of the stellate ganglion to replace the section removed. There has also been an upgrowth of myelinated fibres from the region of the fith thoracic ganglion. However, the arrangement of the outgrowing myelinated fibres is irregular and does not seem to be arranged in any definite pattern. The fibres intermingle with a great deal of fibrous tissue. It has not been possible to demonstrate continuity of the two cut ends. Whether the fibres have established functional communication with the sympathectomised extremity is not known. Further work on this aspect has still to be done.

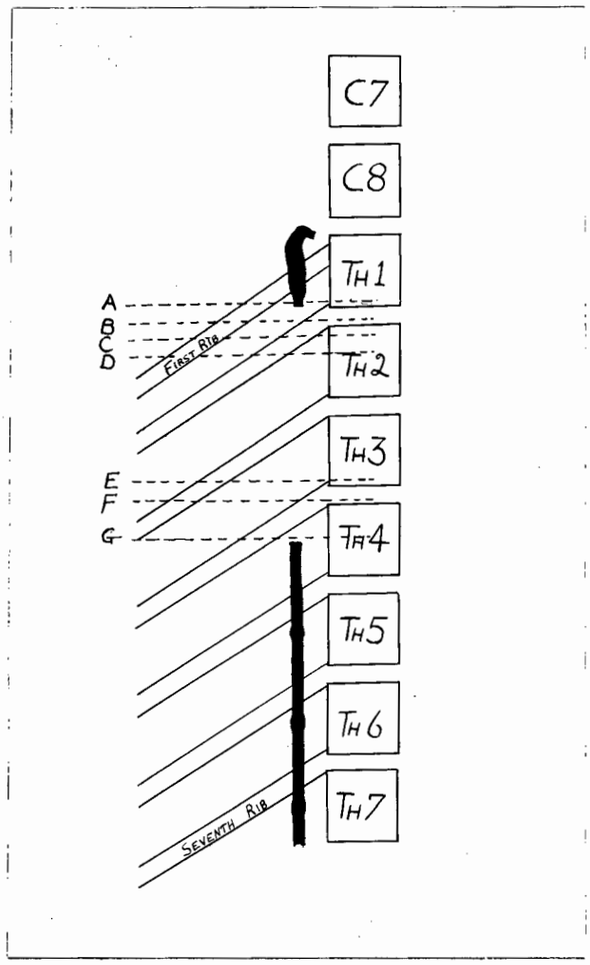


FIGURE 165. - "B"

Schematic representation of the post-mortem findings. Eighteen months after removal of Th.2, Th.3 and Th.4.

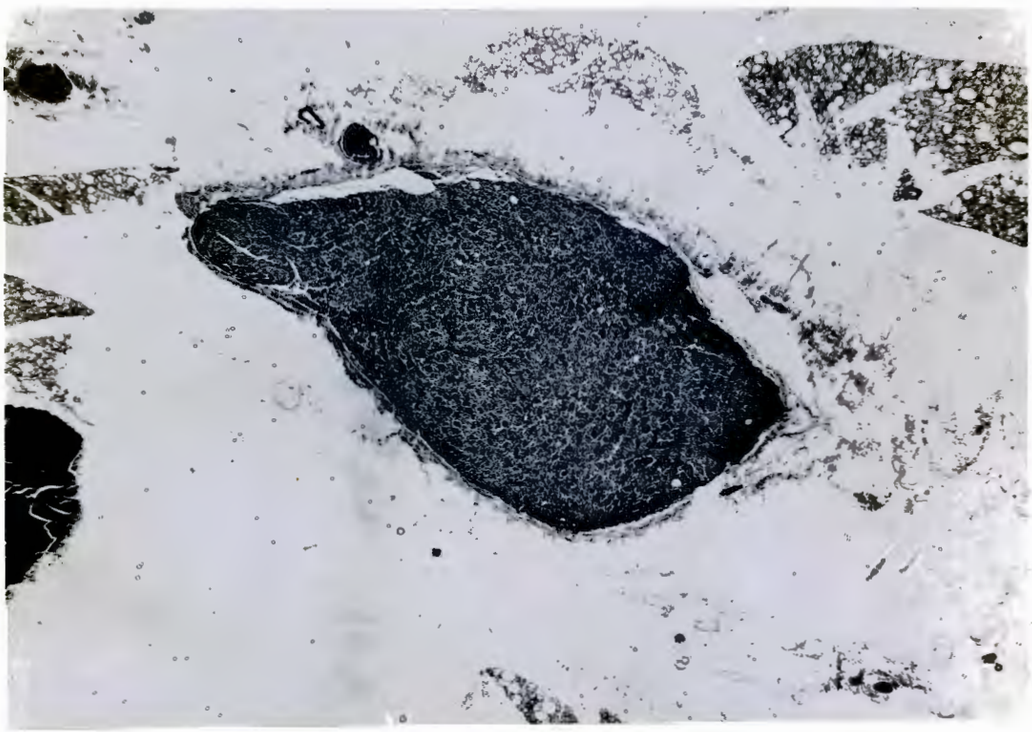


FIGURE 166. - "B"

The left (non-sympathectomised) sympathetic trunk through the first thoracic disc.

X48.5

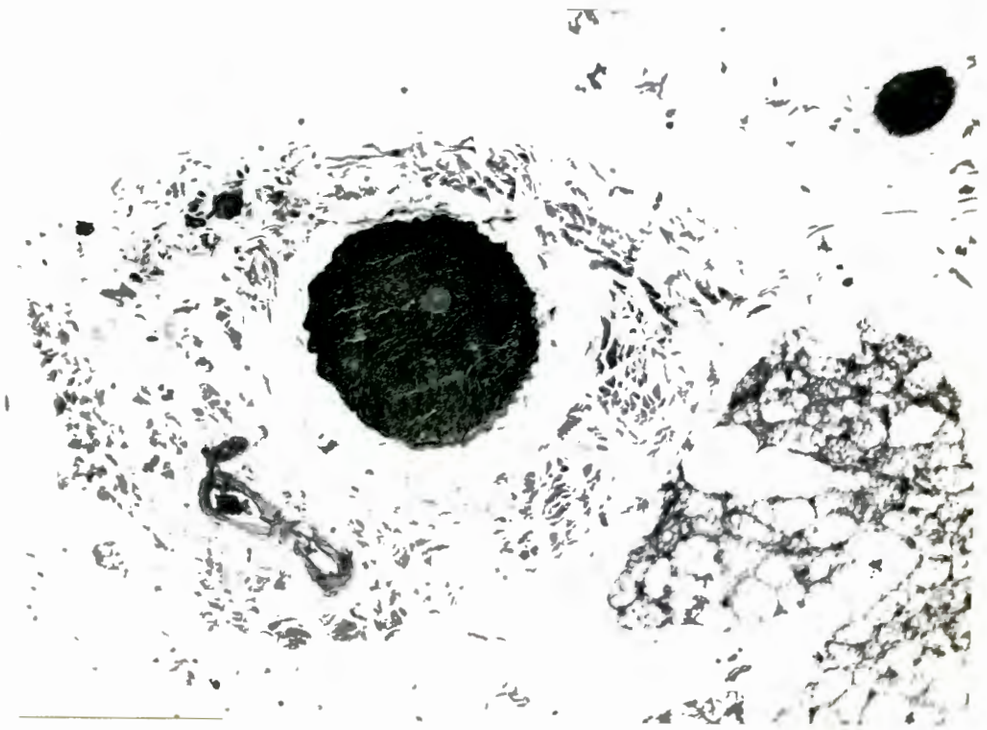


FIGURE 167. - "B"

The left (normal) sympathetic trunk through the third rib.

X233.5

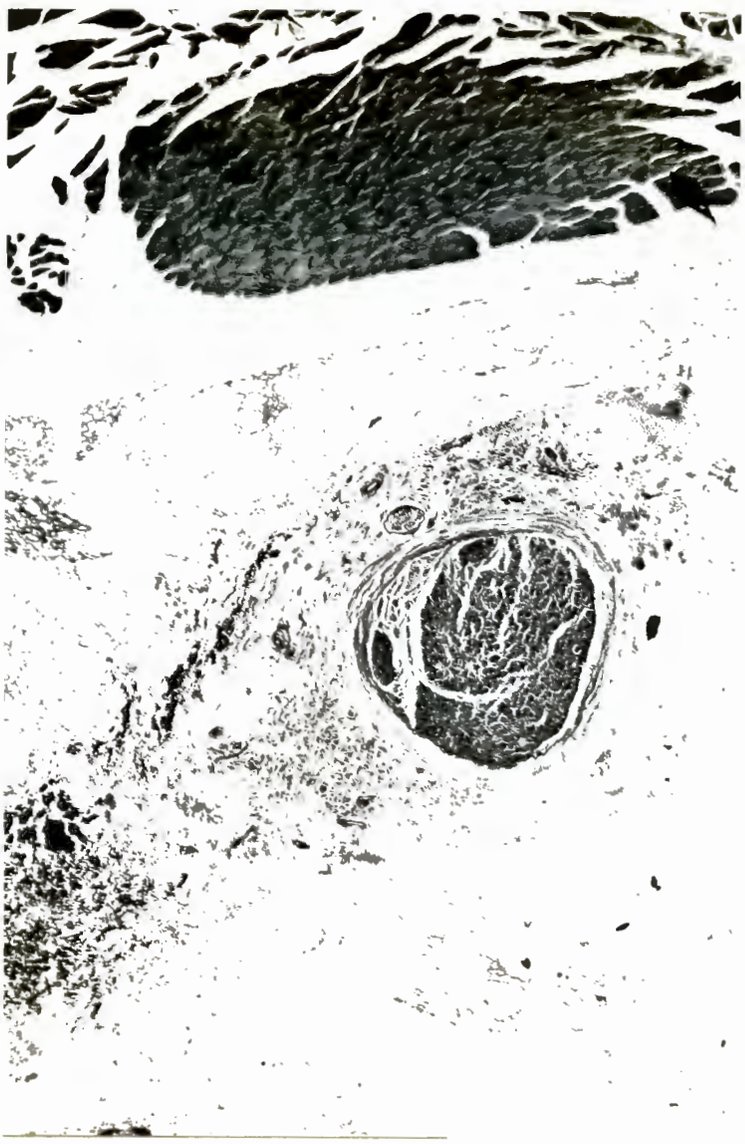


FIGURE 168. - "B"

The right sympathetic trunk at the lower border of the first thoracic vertebra.

(A in Figure 165).

X48.5

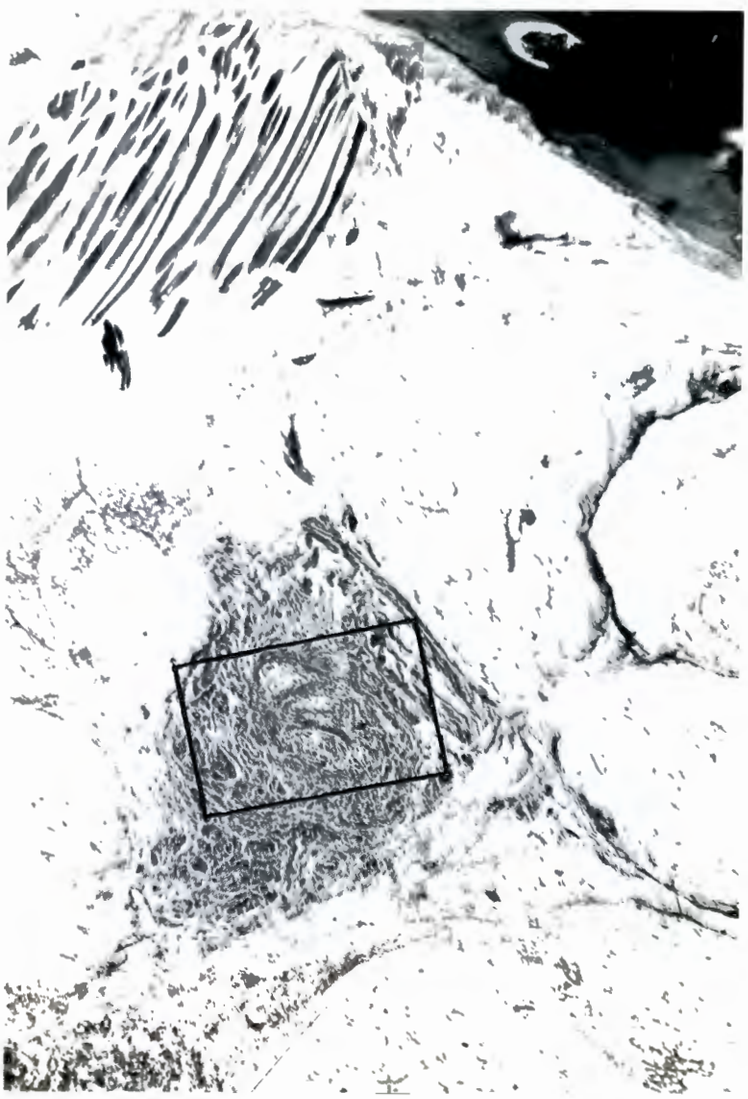


FIGURE 169. - "B"

Section taken through the disc between the first and second thoracic vertebra.

(B in Figure 165).

X48.5

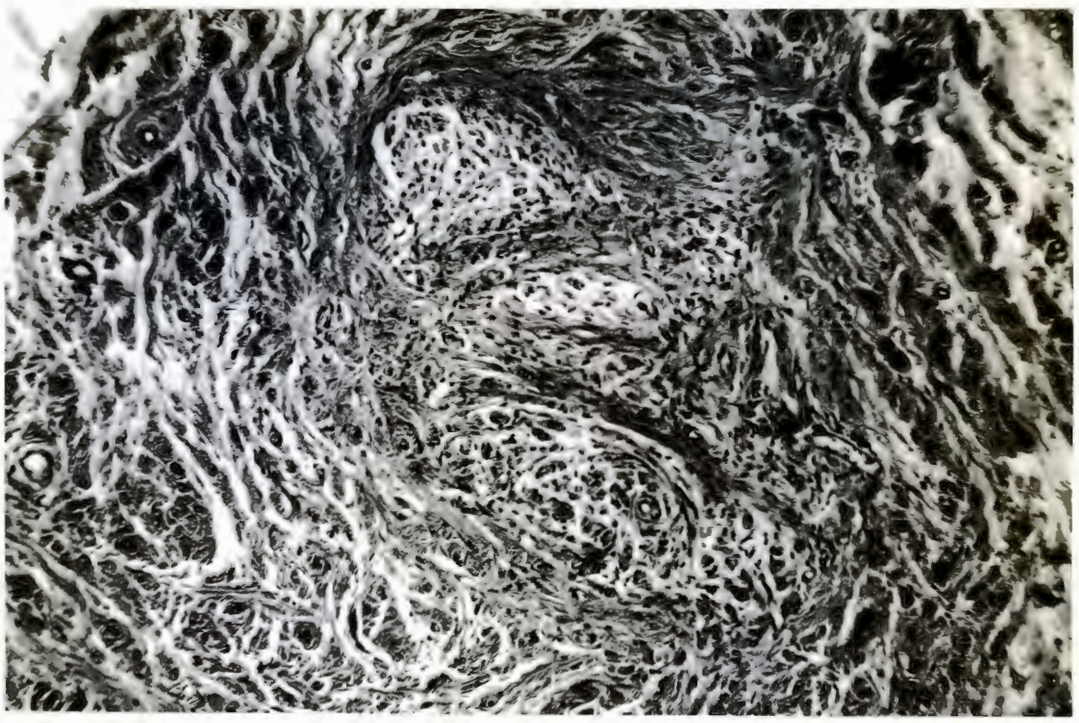


FIGURE 170. - "B"

Inset in Figure 169.

X233.5

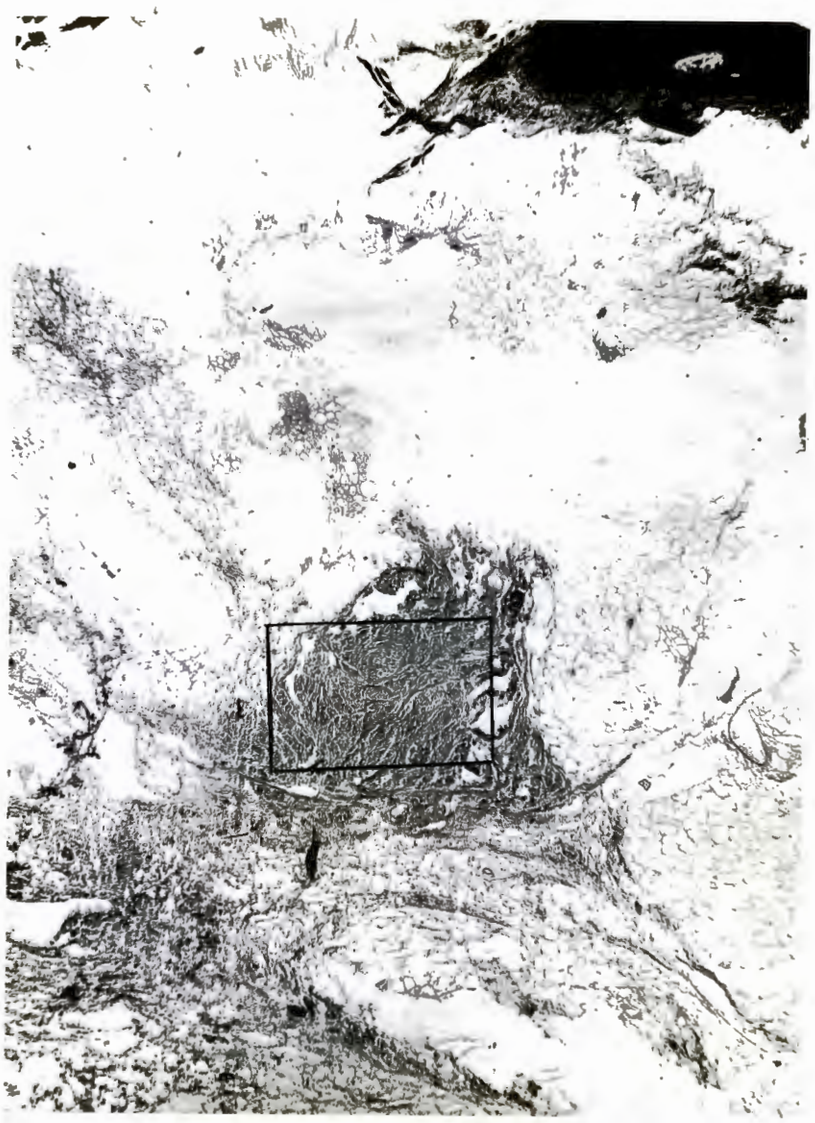


FIGURE 171. - "B"

Section through the upper border of the second thoracic vertebra.

(C in Figure 165).

Romanes' Nerve Stain.

X48.5

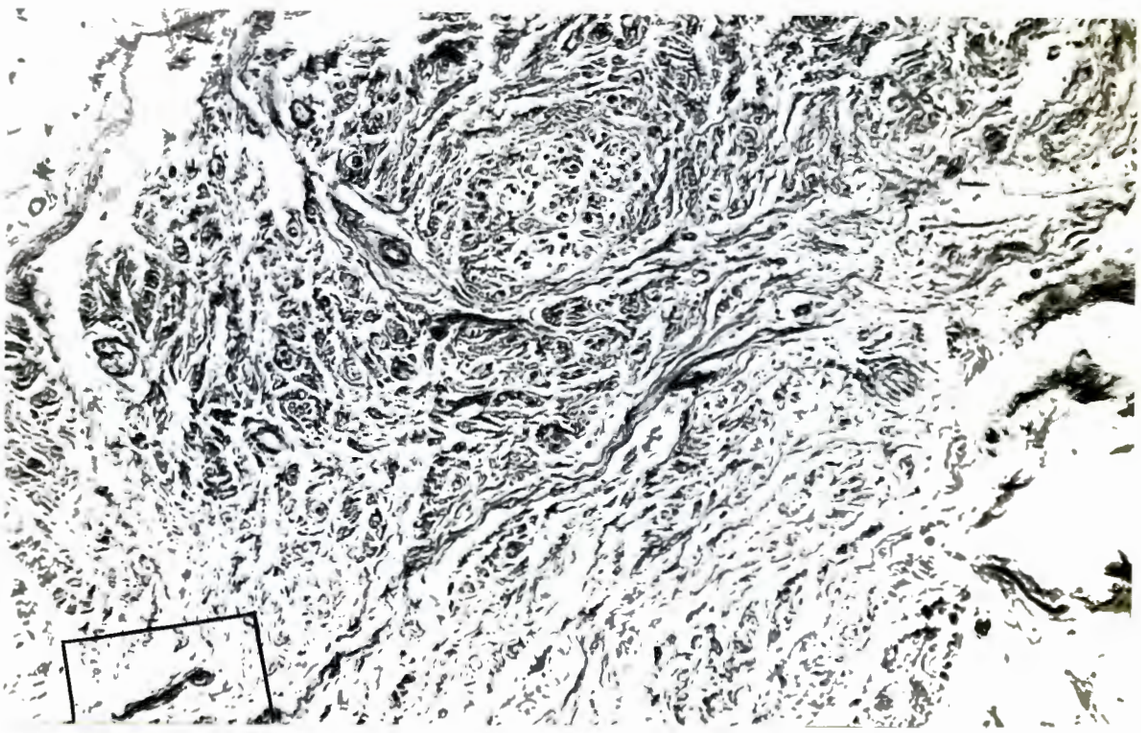


FIGURE 172. - "B"

Inset in Figure 171.

X233.5

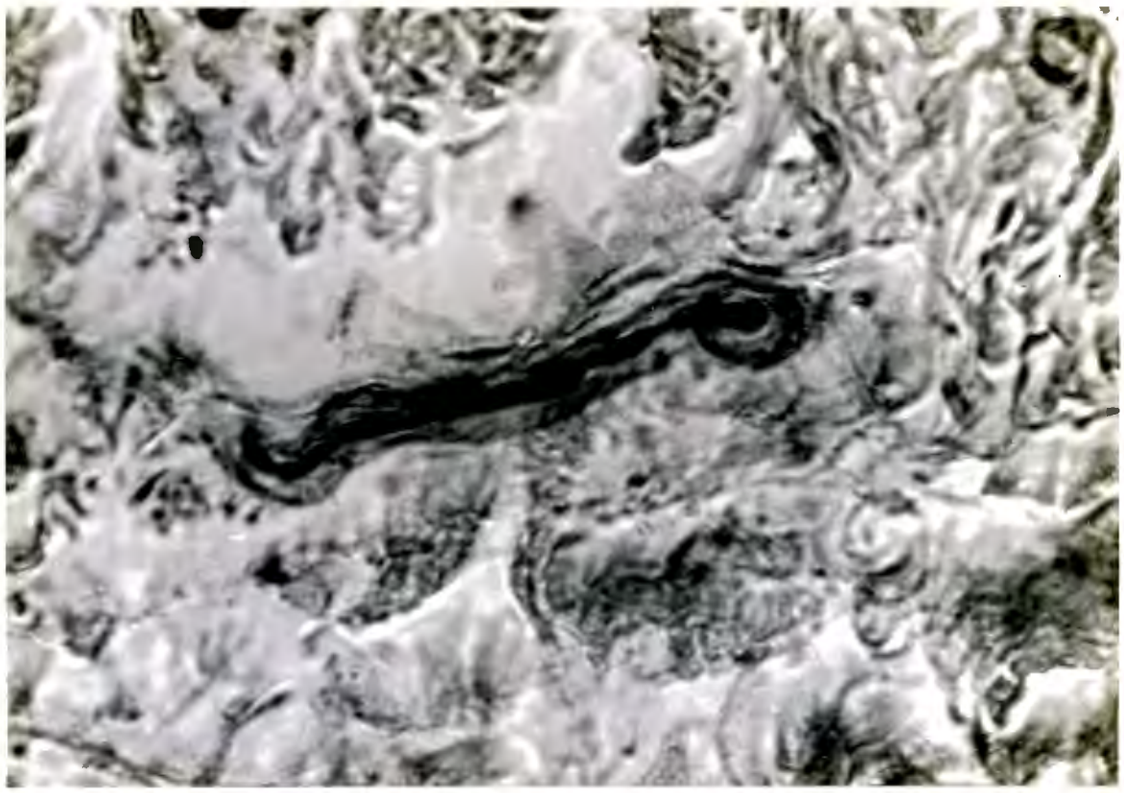


FIGURE 173. - "B"

Inset in Figure 172.

X1280

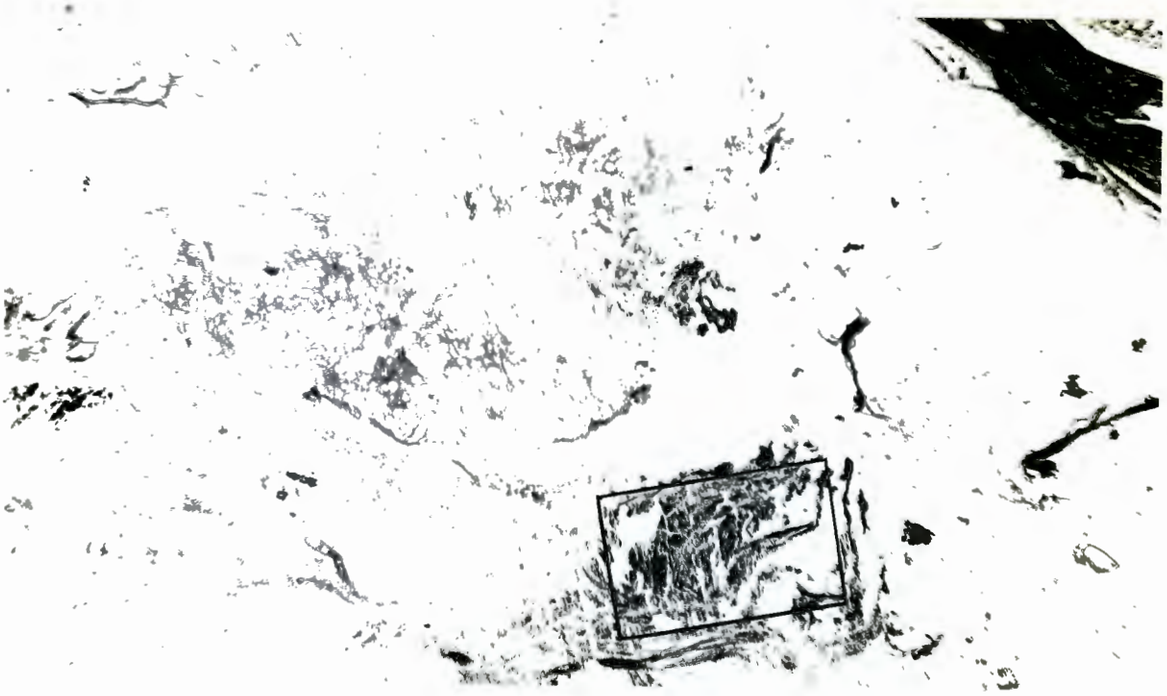


FIGURE 174. - "B"

Section through body of second thoracic vertebra.

(D in Figure 165).

X48.5

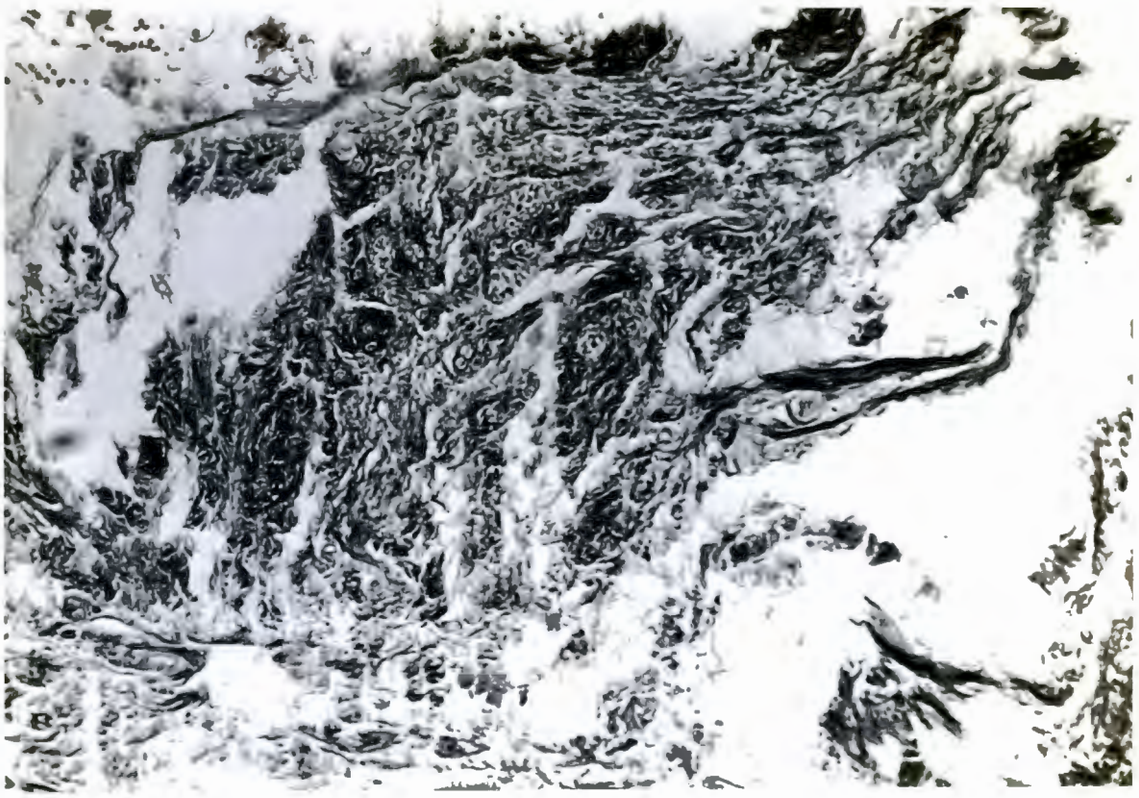


FIGURE 175. - "B"

Inset in Figure 174.

X233.5

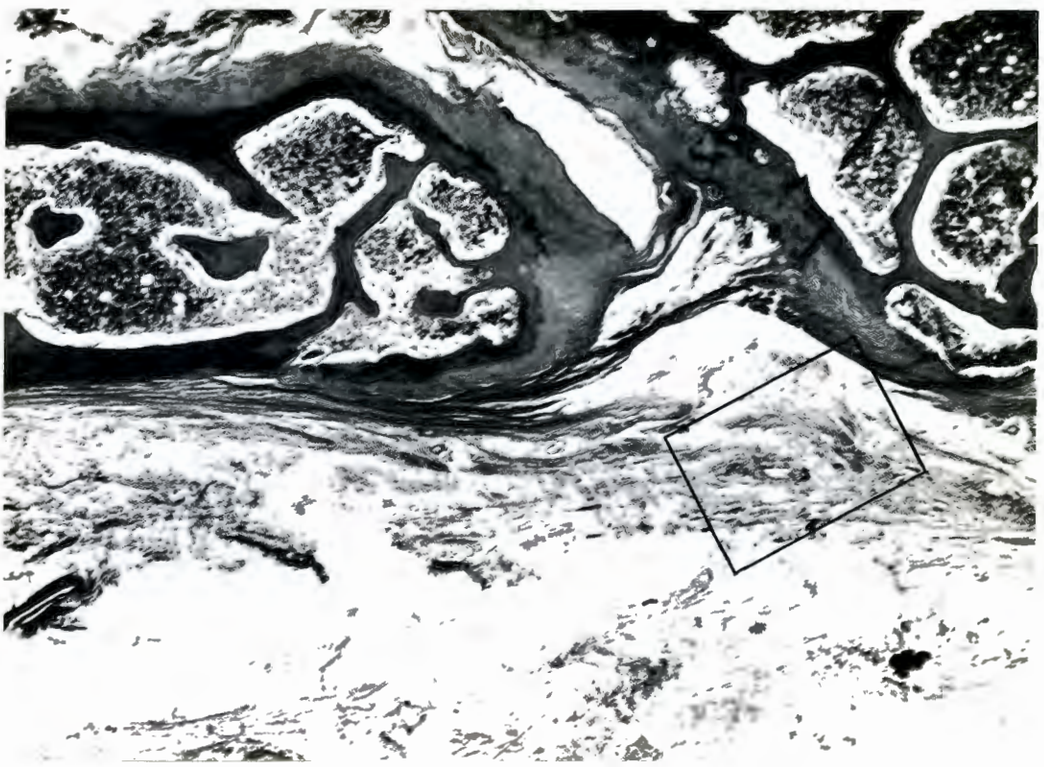


FIGURE 176. - "B"

Section through lower border of third thoracic vertebra.

(E in Figure 165)

X48.5

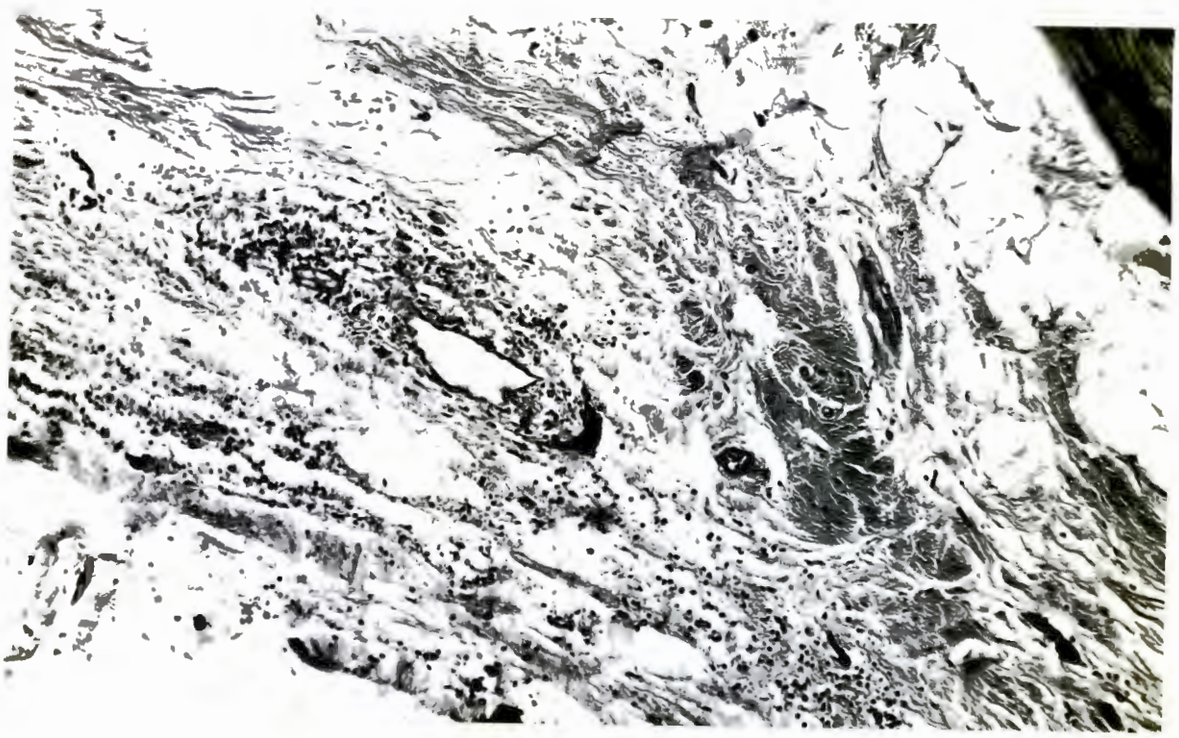


FIGURE 177. - "B"

Inset in Figure 176.

X233.5

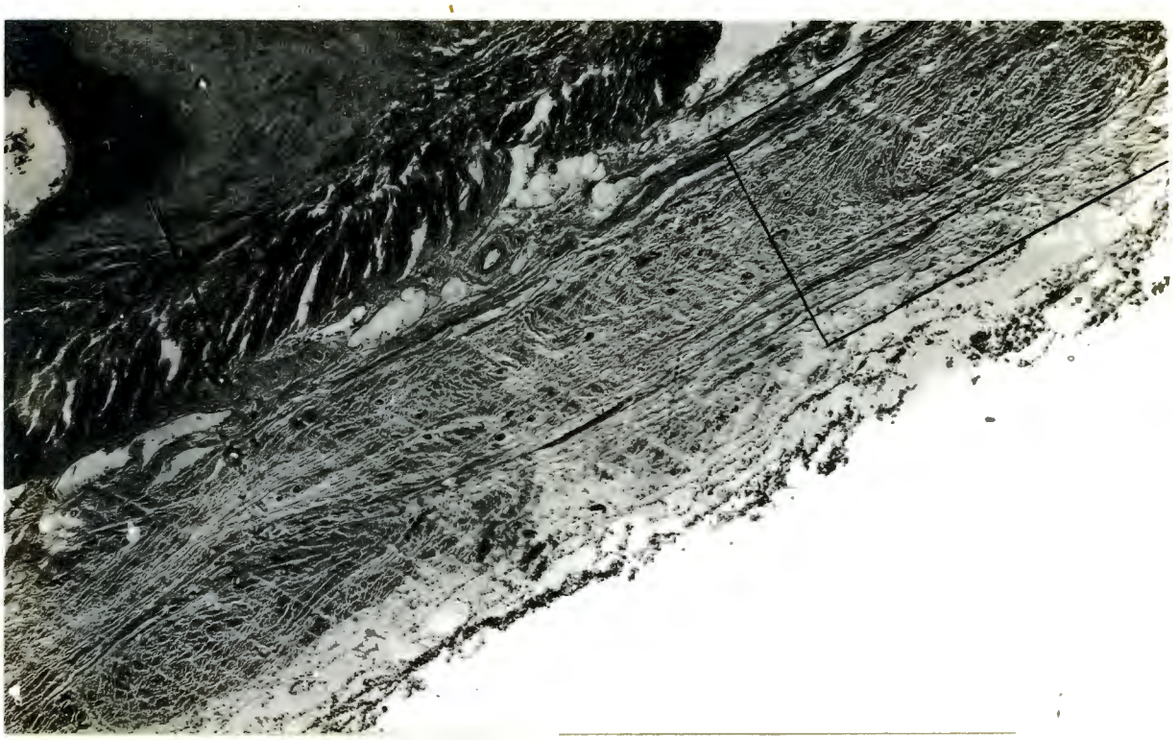


FIGURE 178. - "B"

Section through disc between
third and fourth thoracic vertebrae.

(F in Figure 165).

X93

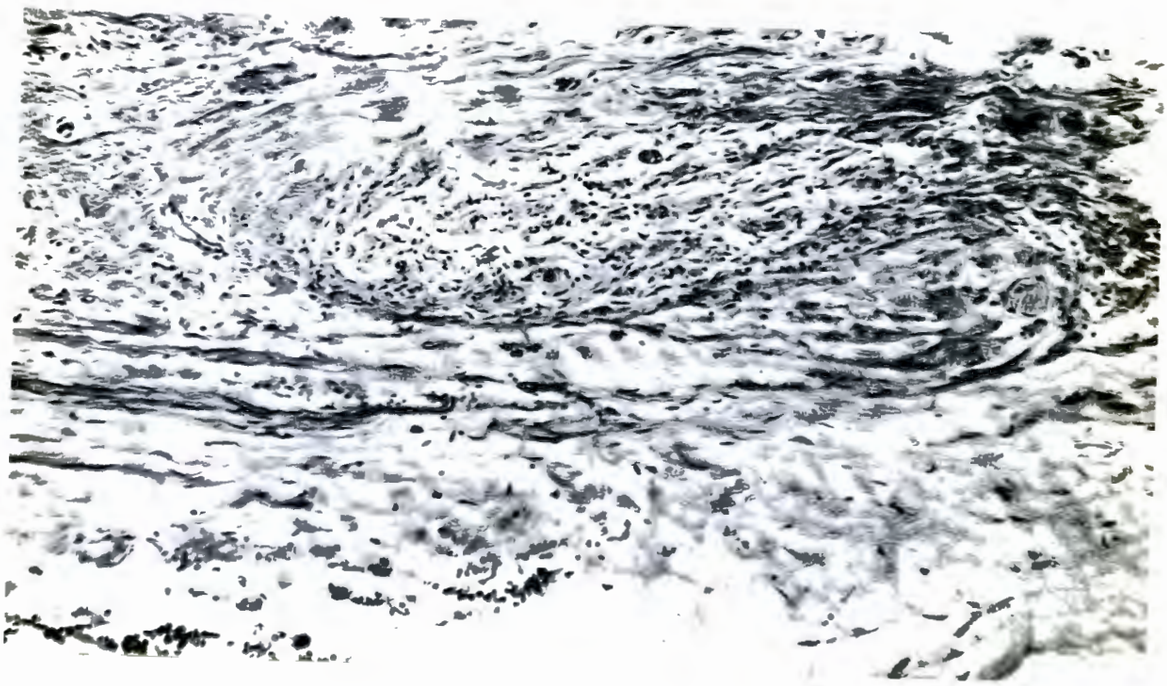


FIGURE 179. - "B"

Inset in Figure 178.

X233.5

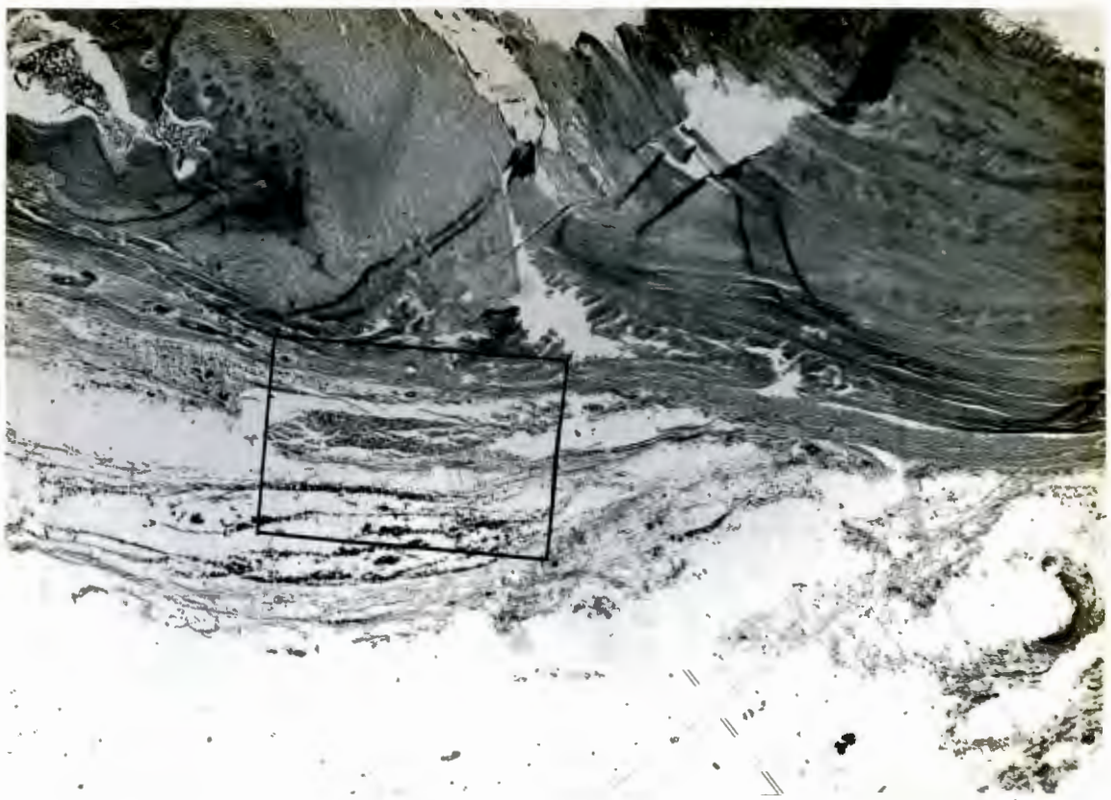


FIGURE 180. - "B"

Section through body of
fourth thoracic vertebra.

(G in Figure 165).

X62.

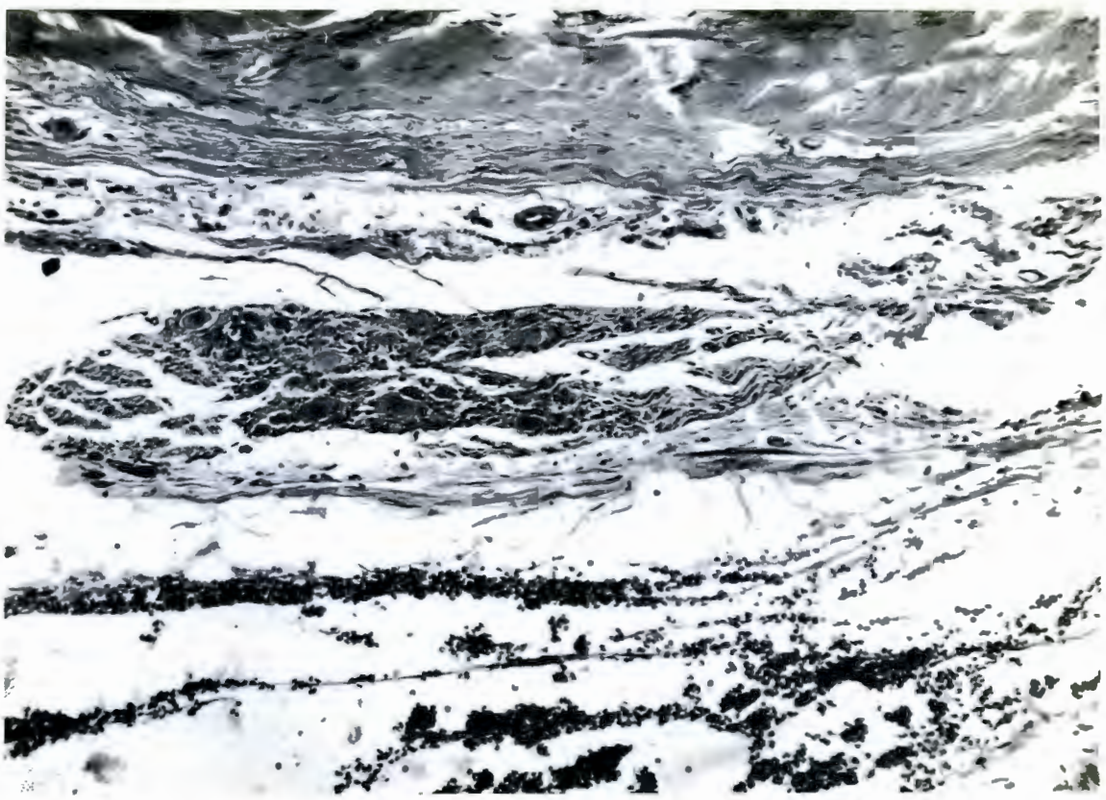


FIGURE 181. - "B"

Inset in Figure 180.

X233.5

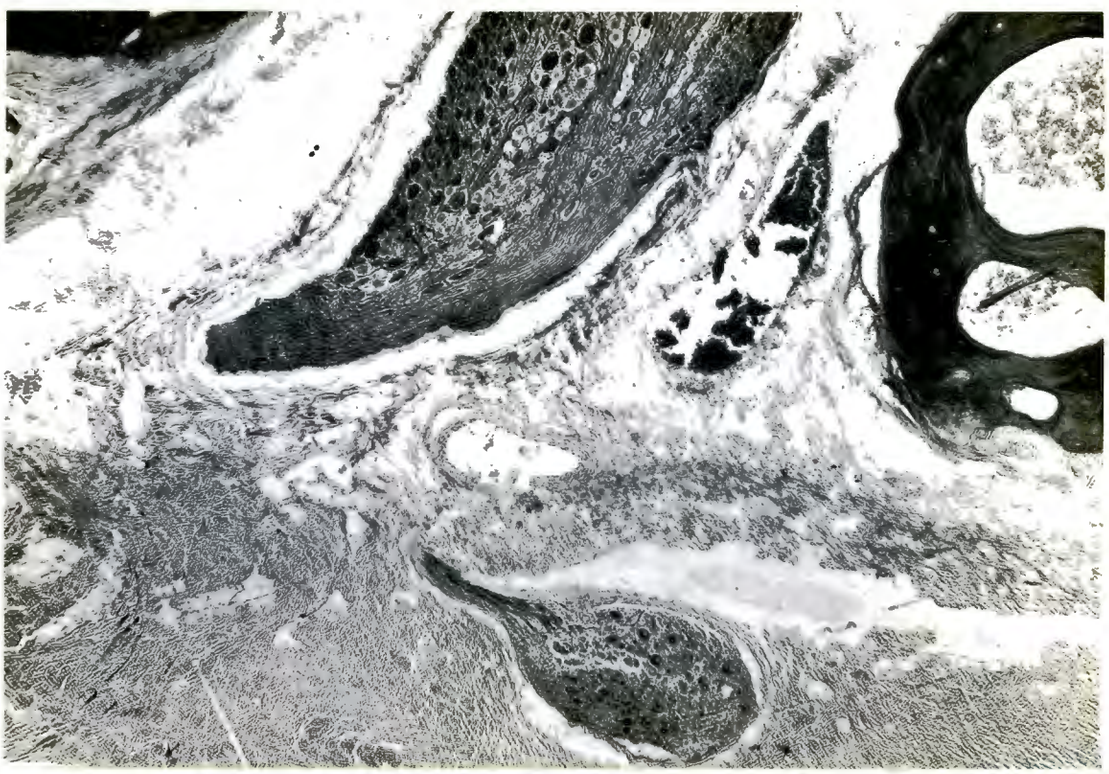


FIGURE 182. - "B"

Section through the sixth thoracic vertebra.

X48.5

V1 DISCUSSION.

It has to be admitted that sympathectomy of the upper extremities has not given the ideal results so easily obtained in the lower limbs. That this only pertains to Raynaud's Phenomena and allied vasospastic disorders is apparent from the results obtained in the present series, for observations on a patient with causalgia, treated by removal of the stellate and second thoracic ganglion thirty years previously, show that the denervation is complete. There has been no return of vasomotor tone or function.

As Craig and Horton (1938) point out, the fact that ganglionectomy applied in the segments corresponding with the upper extremities, is successful in the treatment of Buerger's Disease would seem to militate against the idea of, say, postganglionic sympathectomy producing a sensitivity of clinical importance. In Buerger's Disease ganglionectomy is followed by maximal relief and the results in the upper extremity are, if possible, more satisfactory than those of the lower extremities. Similarly, patients who undergo sympathectomy for other non-vasospastic conditions do not have vasospastic symptoms following the operation.

White (1944) has pointed out that certain fundamentals must be observed by the surgeon in order to get the best clinical results of sympathetic denervation of an extremity. As emphasised by Goetz (1947) the sympathectomy must be:-

1. Preganglionic in type.
2. Anatomically complete.
3. Extensive enough to prevent regeneration and re-establishment of the pathways in the future.

/1. The operation

1. <u>The operation must be preganglionic in type</u> - The spinal centres of sympathetic motor activity are found in the ganglion cells of the lateral horn. The neurones of these cells leave the spinal cord via the anterior root. The corresponding paravertebral ganglia are reached via the white ramus communicans. At the paravertebral ganglia they synapse with the ganglion cells of the second neurone. The axons of the second neurone leave the paravertebral ganglia via the grey ramus communicans to join the spinal nerves and blood vessels. Langley termed the first neurone "the preganglionic fibre", whereas the second is known as "the postganglionic fibre".

Sympathetic denervation thus may be effected by extirpation of the necessary ganglia, by sectioning the anterior root or by dividing the white rami communicantes. However, an essential difference between preganglionic sympathectomy and ganglionectomy was described by Meltzer and Aver (1904) in rabbits, and Meltzer (1905) in cats. They observed that subcutaneous adrenaline had no effect on the normal pupil or upon the pupil denervated by preganglionic sympathectomy, but that it produced maximum dilatation of the pupils denervated by ganglionectomy. Elliott (1905) extended these studies to include the blood vessels and noted that the increased irritability persisted for at least ten months. He also noticed that some degree of increased irritability followed preganglionic sympathectomy.

Dale and Richards (1918) demonstrated that the blood vessels of cats were abnormally sensitive to histamine and acetylcholine as well as adrenaline after sympathectomy.

Freeman et al (1934), using intravenous adrenaline and insulin hypoglycaemia in patients, showed that abnormal

/lowering of the

lowering of the skin temperature developed 68 days after ganglionectomy. Removal of one adrenal and denervation of the other prevented the vascular constriction in animals.

At first surgical intervention on the sympathetic system was based on the experimental observations of Langley that, in the cat, the cervical sympathetic chain and the brachial plexus receive all their preganglionic fibres from the white rami of the middle cervical ganglion. Cervicothoracic ganglionectomy, therefore, appeared to be a means of procuring sympathetic denervation of the arm. Results in Raynaud's Phenomena, however, were not satisfactory.

Smithwick et al (1934) considered the possible relationship of "hypersensitivity" to the recurrence of vascular spasm in Raynaud's Phenomena that often occurred after ganglionectomy. They concluded that hypersensitivity to circulating adrenalin may constitute an important source of unsatisfactory results of sympathetic ganglionectomy for Raynaud's Phenomena.

White, Okelberry and Whitelaw (1936) believed that the difference between upper and lower extremity sympathectomies was that the latter was preganglionic in type. Telford (1935) and Smithwich (1936) thereupon independently performed preganglionic sympathectomy for Raynaud's Phenomena.

Fatheree and Allen (1938) and, later, Fatheree, Adson and Allen (1940), after many carefully controlled experiments, disagreed with the conclusions of Smithwich et al quoted previously.

Simmons and Sheehan (1939), too, are unable to support Smithwick's contentions. They have noted that, after both pre- and postganglionic sympathectomy, the hypersensitivity

/has decreased

has decreased with time. They also observed that hypersensitivity appears at its maximum eight to ten days after operation, whereas the usual clinical relapses are not evident for several months. Further, at the time the relapse is becoming evident, the hypersensitivity to adrenaline is either non-existent, or very much reduced and continually decreasing, whereas the relapse is steadily becoming worse. They also noted that the preganglionic sections which have relapsed have done so sooner than the corresponding ganglionectomies, yet the sensitivity is greater after ganglionectomy than preganglionic section. The occasional permanently successful result following ganglionectomy is unexplained by hypersensitivity.

Lewis, too, has pointed out that, if recurrence of symptoms is due to hypersensitivity to circulating adrenaline, the attacks of Raynaud's Phenomena should occur equally after sympathectomy whether the patients operated on had the Raynaud's Phenomena or not. This certainly does not occur.

As Fatheree et al conclude: "The problem of unsatisfactory results that occasionally follow operations for Raynaud's Phenomena of the hands has not been satisfactorily solved by a study of sensitivity of digital arterioles to adrenaline." This conclusion is in agreement with the opinion of many surgeons and Grimson (1946) observes that these unsatisfactory results have not been materially solved by operations employing the preganglionic sympathectomy technique.

Goetz (unpublished data) has been investigating the problem of sensitivity to adrenaline following pre- and post-ganglionic sympathectomy, plethysmographically. Utilising the photo-electric-cell drop-recorder (Goetz - 1948), he has administered adrenaline to many of the patients observed in

/this series.

this series. Without finalising, the impression is gained that Fatheree et al's observations are correct.

2. The operation must be anatomically complete -

The work of Simeone, Cannon and Rosenblueth (1938) and Simeone (1938) has shown that incomplete denervation of any structure which is under the control of the autonomic nervous system, results in little functional impairment. Surgical denervation must be complete or it will be of little value. The entire sympathetic outflow from the spinal cord to the organ or the extremity must be interrupted, or any pathway left uninterrupted can be used by the body to re-establish complete sympathetic control within a short period.

The origin of the preganglionic fibres to the upper extremity is still a matter of considerable dispute. Although the second thoracic spinal segment is commonly accepted as the uppermost limit of outflow of preganglionic fibres to the upper extremity, there is no doubt that a large number of myelinated fibres leave the spinal cord from the lower cervical regions. Ray et al (1943) had occasion to stimulate the anterior roots in man and found an outflow from Th.1 in one of eleven patients.

Also, it has been found that if the brachial plexus be pre-fixed, the uppermost limit of outflow from the spinal cord will be from the eighth cervical nerve.

The segmental outflow of vasoconstriction and sudomotor fibres may extend quite a long way caudally, and, in some cases, the lowermost level has been as far caudally as Th.8 - Th.10. However, the uppermost level is the most important.

The preganglionic fibres from the spinal cord enter the paravertebral ganglia at their corresponding points and

/ascend in the

ascend in the chain. These preganglionic fibres synapse with the postganglionic neurone mainly in the inferior cervical and first thoracic ganglia, i.e. the stellate ganglion. Few synapses are said to occur in the second and third thoracic ganglia.

Whilst the majority of synapses of preganglionic fibres with the postganglionic neurone occur in the above three ganglia, it appears likely that synapses of preganglionic fibres to the upper extremity are made in the middle cervical ganglion as well. The middle cervical ganglion usually is connected through grey rami with the fifth and sixth cervical nerves and, in some instances, with the fourth and seventh. cervical nerves.

Foerster also found that stimulation of the middle cervical ganglion produced vasoconstriction in the upper extremity of the corresponding side.

As Fatheree et al (1940) observe, it appears unlikely that the sympathetic fibres which supply the upper extremity of man make synapses in ganglia other than the middle cervical, the stellate and the second thoracic ganglia.

de Takats (1937) observed that "the complete removal of the ganglionated trunk with its postganglionic fibres can show evidence of regeneration only if the operation did not remove all the excitor ganglions and if some postganglionic fibres escaped section, or, if a preganglionic section of the trunk was carried out, after which the preganglionic fibres readily established connection with the intact ganglions and their postganglionic fibres." At a later date (1940) he suggested extending the original (postganglionic) cervico-thoracic sympathectomy to include the intermediate and inferior cervical as well as the first, second and third thoracic ganglia.

/In sixteen

In sixteen cases in which he followed this procedure, the results were, in his opinion, comparable with those obtained from lumbar sympathectomy.

In this way de Takats actually attempts to remove all sympathetic connections to the brachial plexus. In essence this is a postganglionic sympathectomy, which, as we have seen, is not of great importance.

In 1942 Geohegan and Aidar suggested that the recovery of sympathetic tone may be due to reorganisation of function within the sympathetic itself. Ray et al (1942) had observed a case in which the ventral roots from the second to the ninth thoracic segments were sectioned. This resulted in complete sympathetic denervation of the hand. However, after ten weeks, function returned. This could not have been due to regeneration because of the short time interval. They suggested that pathways were being used which, before operation, did not carry sympathetic impulses to the hand. The first thoracic root, which ordinarily carries no vasoconstrictor fibres to the upper extremity, may develop such function after the usual pathways have been interrupted. From the work of Pick and Sheehan (1946) the presence of myelinated fibres in the lower cervical roots is well known. Geohegan and Aidar put this theory to the test and found that, after interruption of all preganglionic fibres to the forepad in the cat, new pathways developed from higher spinal roots which normally contribute no outflow to the upper extremities.

These findings are interesting in view of de Takats' effort to remove all sympathetic connections to the brachial plexus, in order to establish a complete sympathetic denervation of the upper extremity.

von Buskirk (1941), examining the sinuvertebral nerve running inside the vertebral canal, considered that he had

/demonstrated

demonstrated a pathway through which sympathetic fibres arising at lower levels might join the upper thoracic and lower cervical nerves. However, the ramus connected to the vertebral artery usually arises from the stellate ganglion, which is extirpated in de Takats' operation.

Skoog (1947) has demonstrated ganglia in the communicating rami of the cervical sympathetic system. However, it is not known whether these ganglion cells receive their preganglionic fibres from the sympathetic trunk or from the spinal nerves. Wrete (1935), basing his theory on the embryology, thinks that, in the lumbar region, where these ganglia also occur, most of the ganglia probably migrate from the sympathetic trunk. If the latter pertains then complete sympathectomy is impossible. If, on the other hand, these are sympathetic connections, then ganglionectomy will still be complete with de Takats' procedure.

3. <u>Sympathetic denervation must be carried out in such a way as to prevent regeneration</u> -

As early as 1895 Langley had observed that regeneration of preganglionic fibres may take place by the formation of fresh terminations in connection with nerve cells. He observed in cats, by cutting the sympathetic chain in the neck, that return of function began eight to twelve days after operation, and that, in the majority, the cervical sympathetic had regenerated in twenty-four days after section. He noted that some deficiency of innervation after regeneration was almost inevitable. Nevertheless, the deficiency was not striking and, in most cases, slight.

Previously Pye-Smith (1887) reported recovery of

/control of the

control of the eye and temperature of the ear in a cat 110 days after removal of a portion of the cervical sympathetic chain.

Langley (1897), Tsukaguchi (1916) and Lee (1929) have established the ability of preganglionic fibres in cats, dogs and rabbits to regenerate. Lee (1929) observed regeneration even through the sternomastoid muscle. Hinsey, Phillips and Hare (1938) demonstrated preganglionic regeneration to the head and limbs of cats after various forms of sympathectomy.

The ability of postganglionic fibres to regenerate has also been investigated. Tuckett (1896) obtained evidence of regeneration of postganglionic fibres from the superior cervical ganglion of a rabbit in 259 days. Machida (1929) found evidence of regeneration in cats, as early as fifty-seven days, and also noticed that vasomotor recovery preceded recovery of the pupil. Kilvington and Osborne (1907) demonstrated return of vasomotor reflexes plethysmographically in dogs. Trotter and Davies (1909) reported varying degrees of recovery of sudomotor and pilomotor functions six to eight months after peripheral nerve section performed upon themselves.

Gibson (1940), who has made a microscopic study of the sympathetic synapse, has observed degeneration of the boutons (fibre terminations on the nerve cells) in the superior cervical ganglion after proximal section of the trunk, and their reappearance with a return of function forty-four days later.

Haimovici and Hodes (1940) have presented evidence for regeneration even after removal of the entire sympathetic chain on both sides.

/Simmons and Sheehan

Simmons and Sheehan (1939) and Smithwick (1940) have observed many instances of recurrent vasomotor activity after cervicothoracic ganglionectomy. How preganglionic axons can bridge the gap left by the removal of the cell-bodies of the postganglionic neurons is difficult to understand ! No histological explanation has yet been given, but numerous tests show that a greater or lesser degree of regeneration is evident in a larger proportion of patients.

Papez, Jensen and Dukes (1945) observed two dogs after thoraco-lumbar and splanchnic nerve sympathectomy. They noted that regeneration after such a procedure is relatively small. They also observed that some of the pre-ganglionic neurones in the intermedio-lateral cell column of the spinal cord survive the operation and are capable of regeneration. The regenerating fibres tend to course along the older channels that are partially restored by the pre-cocious regeneration of perineural sheaths.

Haxton (1947a) considers that regeneration is responsible for the return of symptoms and vasomotor tone in Raynaud's Phenomena. In a later paper (1947b) he describes the autopsy findings in a case of Raynaud's Phenomena, who had had the left stellate and second thoracic ganglia removed fifteen years before. Haxton found that rami were present to all the spinal nerves and a large ganglionic mass was present at the site of the normal stellate. In fact, he observes that the only difference between this and the normal side was the presence of scar tissue on the side of operation! Clinically the patient had suffered a relapse shortly after operation.

In the later article Haxton observed that the permanent Horner's Syndrome is not evidence against regeneration.

/In his experience

In his experience it is only the ptosis that persists and this he ascribes as due to disuse atrophy of the smooth muscle fibres of the levator palpebrae superioris. The miosis, according to Haxton, does not persist. However, in the patient still sympathectomised after thirty years, both the ptosis and miosis are still present.

Although regeneration may be the cause of relapse in the upper extremity, poor results are very seldom noted in the lower extremity. However, Smithwick (1940) observed that almost as many cases have regenerated in the lower extremity as in the upper extremity. Haxton (1947a) too, observed that lower limb results were by no means perfect and some cases of severe relapse were seen. Haxton (1947b) noticed, in the autopsy mentioned above, that regeneration had taken place after lumbar sympathectomy. Although no ganglia were demonstrable, the sympathetic chain was continuous, albeit much thinner at the area of operation.

Confirmation of regeneration, occurring after sympathectomy, is obtained by the observation of the sympathectomised monkey "B". Although macroscopically no connection was visible between the cut ends of the sympathetic chain, evidence of regeneration was present microscopically. Nerve fibres are present in the midst of a vascular connective tissue, both from the caudal and cranial parts of the sympathetic chain. That these fibres were neural in origin was shown by use of Romanes' modification of the silver nitrate stain. However, these regenerating fibres had not established functional connection with the vessels of the extremity.

Thus, although regeneration may occur, theoretically it is more difficult to imagine after ganglionectomy, than after preganglionic section. If all the postganglionic cell

/stations to the

stations to the arm have been removed at operation then either preganglionic fibres grow up and pass directly into the nerves of the brachial plexus, or, what appears to be more likely, postganglionic fibres, whose cell stations are situated below the level of excision, regenerate through the scar tissue to reach the nerves of the upper extremity.

Haxton (1947a) observes that, although all cases of clinical relapse show regeneration of sympathetic fibres, this is not the whole explanation of relapse. Well-marked regeneration may occur without any clinical relapse and complete relapse may develop in spite of very incomplete regeneration. Also, although regeneration of sympathetic fibres and a return of activity in the lower limb occur more frequently than realised, the extremity is almost completely free from clinical relapse. Although only the upper limb has been investigated in this series, clinical relapse of Raynaud's Phenomena is a rarity in the lower extremities. Numerous sympathectomies have been performed for Raynaud's Phenomena of the lower limbs, yet not one case has been observed with a clinical relapse. As judged plethysmographically, a return of vasomotor tone is present in only one case of the lower limb. (Figure 78. - page 251). Sudomotor activity is, however, still absent in this extremity.

Haxton (1947) explains clinical relapse as due to the fact that two factors are important in the production of Raynaud's Phenomena, viz. sympathetic vasoconstrictor activity and local sensitivity to cold. These two factors vary considerably in different cases. Sympathetic activity predominates in those cases where fear or excitement produce spasm. These are the cases which should do well after

/operation

operation. However, the association of spasm with these vasoconstrictor reflexes is not common.

Far more frequently spasm occurs on exposure to cold. Haxton claims that these cases with a marked local sensitivity to cold cannot be expected to give good results.

Between the two extremes are the vast majority of cases, in which both vasoconstrictor tone and local sensitivity to cold play a part and the results of operation vary according to which is the predominant symptom. Haxton concludes that this dual mechanism explains satisfactorily how cases can show well-marked regeneration without relapse or can relapse badly with only a slight return of sympathetic activity.

It is apparent, therefore, that only two factors need be considered in determining the method of sympathectomy of the upper extremity. The operation must be anatomically complete and it should be extensive enough to prevent regeneration. That the difference between pre- and postganglionic sympathectomy is not responsible for the recurrence of symptoms appears certain from the discussion above.

Sympathetic denervation of the upper extremity, as practised at Groote Schuur Hospital in the past, leaves the stellate ganglion and all its communicating branches to the brachial plexus intact. Apart from the difference in pre- and postganglionic sympathectomy, stellatectomy has not been practised because of the resulting Horner's Syndrome.

Horner's Syndrome, however, is not as disfiguring as generally accepted. Ptosis is maximal for eight days after operation. Thereafter, an improvement results, and, in most cases, is barely noticeable unless expressly looked for. Also, if bilateral stellatectomy is performed Horner's

/Syndrome

Syndrome is usually equal on the two sides and cosmetically the difference is hardly noticeable. It is the experience at Groote Schuur Hospital that Horner's Syndrome is less obvious after removal of the middle cervical ganglion as well. Therefore, there is really no contra-indication to removing the stellate ganglion. In fact, there appears to be every reason for removing the ganglion and all its branches to the brachial plexus.

Although relapse after sympathectomy of the upper extremity, by removal or cauterisation of the second thoracic ganglion, usually takes place twelve to eighteen months after operation, two cases are included in the present series, in which, after removal of the second, third and fourth thoracic ganglia, return of symptoms has taken place within six months. Regeneration is unlikely to explain the relapse in these cases.

The reason for relapse may well be that operation is incomplete or that, as Geohegan and Aidar (1942) suggest, reorganisation has taken place and that myelinated fibres, previously not concerned with innervating the upper extremity, assume the function of the interrupted pathways. It is more than likely, however, that operation is incomplete.

In order to make the sympathectomy as complete as possible, all the communicating fibres to the brachial plexus must be removed. Therefore, the middle cervical ganglion, through its rami to the fifth and sixth cervical nerves, must be included in the tissue removed. Caudally, the second and third thoracic ganglia should be included as well. If possible, removal of the fourth thoracic ganglion is advised.

Simmons and Sheehan (1939) have pointed out that, theoretically, regeneration is less likely after ganglionectomy than after preganglionic sympathectomy. Therefore, removal

/of the above

of the above structures is less likely to be followed by regeneration. Support is added to this theory by the demonstration of the case observed thirty years after operation.

/VII. SUMMARY.

VII. SUMMARY.

(1) The history of our knowledge of the sympathetic nervous system and the relationship with the endocrine system and humoral factors is discussed.

(2) The anatomy and physiology of the sympathetic supply to the upper extremities is described. Special emphasis has been placed on the apparent failure to produce a lasting sympathectomy of the upper extremity. Possible anatomical and physiological reasons for this are considered.

(3) The effect of removal of the sympathetic supply of the vessels of the upper extremity is discussed.

(4) A review of Raynaud's Phenomena is presented. Factors in the symptomatology and pathology are considered. The failure of treatment of Raynaud's Phenomena of the upper extremities is examined.

(5) A study is made of the treatment of Raynaud's Phenomena by sympathectomy. The various methods attempted to produce complete and lasting sympathetic denervation of the upper extremities are considered.

(6) The effect of sympathectomy of the upper extremities in Raynaud's Phenomena is estimated.

(7) An investigation has been conducted into the results of sympathectomy of the upper extremity, as performed at Groote Schuur Hospital. The methods used are outlined and the results analysed.

/(8) The case

(8) The case histories of all patients examined are presented. The results of pre- and post-operative tests are detailed.

(9) The anatomy and physiology of the sympathetic nervous system in the monkey is described. The similarity between the human and the monkey is commented on.

(10) The method of sympathectomy in the monkey is outlined. Special mention is made of the means of determining the extent of sympathectomy by electronic stimulation. At the same time the extent of the sympathetic supply to the upper extremity is noted.

(11) The post-operative course in monkeys is observed and the findings described at re-operation at varying periods after sympathectomy.

(12) The post-mortem findings are detailed in one monkey eighteen months after sympathectomy. Both macroscopic and microscopic details are observed.

(13) A discussion ensues on the method of producing lasting sympathectomy of the upper extremity in Raynaud's Phenomena. The conclusions drawn therefrom are analysed.

/VIII. CONCLUSIONS.

VIII. CONCLUSIONS.

Preganglionic sympathectomy of the upper extremity in patients with Raynaud's Phenomena has not resulted in permanent cure in those cases observed over a period of time.

Sympathectomy was undertaken either by cauterisation or by open thoracotomy. Return of symptoms or evidence of vasomotor tone has taken place irrespective of the method of operation. However, return is more likely to occur following cauterisation.

The second thoracic ganglion is regarded as the main outflow of sympathetic fibres to the upper extremity. Although the immediate results of removal of this ganglion are good, later results are not satisfactory.

Caudal extension to include the third and fourth thoracic ganglia also has good immediate results. The later results are not complete. Nevertheless, vasoconstriction has been produced in one case within a year after operation. It is possible that the late results of this procedure will be no better than removal of the second thoracic ganglion only.

The time of relapse after operation is variable. Some cases show a return of symptoms within a few months. It is likely that these relapses are due to incomplete operation.

Most cases relapse one year or more after operation. Tests indicate that, although sweating may return, it does not return to the pre-operative state. Patches of anhidrosis may persist.

The recurrence of symptoms after sympathectomy cannot be explained by a hypersensitivity to adrenaline.

/recurrence of

Recurrence of symptoms may be due to regeneration. This is more likely in the late recurrence but cannot explain the early relapses. Should regeneration be the responsible factor, such regeneration is incomplete.

Should regeneration be responsible for the return of vasomotor tone, the fact that the actual cause of the spasm is a local fault of the digital vessels, which would persist despite operation, is not excluded. The re-establishment of vasomotor tone by regeneration would precipitate spasm in such abnormal vessels, but not in cases where no local fault existed in the first place.

It had been shown that regeneration is more likely after preganglionic section than after ganglionectomy. A case of causalgia is reported showing absence of vasomotor tone in the upper extremity thirty years after removal of the stellate and second thoracic ganglia. In this case regeneration has certainly not occurred.

Electronic stimulation of the sympathetic paravertebral ganglia in monkeys shows that the main supply to the upper extremity occurs from the stellate and second, third and fourth thoracic ganglia. In one monkey the lowermost limit was the sixth thoracic ganglion.

Electronic stimulation of the sympathetic paravertebral ganglia in one patient with Raynaud's Phenomena shows that the stellate and second, third and fourth thoracic ganglia are the source of supply to the upper extremity.

In monkeys pupillary fibres were derived from the stellate ganglion only, whereas in one patient stimulation of the second thoracic ganglion resulted in pupillary dilatation.

Electronic stimulation furnishes a means of determining the completeness of sympathectomy at the time of operation.

/Histologic

Histologic examination of the sympathetic chain, in a monkey eighteen months after removal of the second, third and fourth thoracic ganglia, shows that there has been a downgrowth of nerve fibres from the cranial end and also a scanty upgrowth from the caudal end. No communication between the two ends could be demonstrated. It is possible that communication might have been established had a further period elapsed before death of the animal. No ganglion cells were demonstrable in the sympathectomised area.

Therefore, it has been demonstrated that regeneration of the sympathetic can occur in the monkey after preganglionic section.

Whilst no hard and fast rule can be laid down as to the indications for sympathectomy in Raynaud's Phenomena, most patients who have undergone the operation observe that improvement has occurred. Thus, although the late results of operation show clinical relapse to be fairly common in the upper extremities, sympathectomy has been worthwhile in the great majority of patients.

Sympathectomy should be reserved for those cases where the condition is a handicap to the patient either socially or economically. The majority of patients with cold extremities may be able to get along by avoidance of exposure to cold water or air or by the wearing of warm clothing. Should, however, these measures prove inadequate operation should be resorted to.

In order to minimise subsequent regeneration and also to ensure a good immediate result, resection should be

/as extensive

as extensive as possible. There are no contra-indications to ganglionectomy and, therefore, the operation should include the middle cervical, the inferior cervical and the first thoracic ganglia (representing the stellate ganglion) together with the second and third thoracic ganglia. In this way all sympathetic connections with the brachial plexus are severed and operation can then be termed complete.

/IX. RECOMMENDATIONS

IX. RECOMMENDATIONS FOR FURTHER STUDY.

Several features arise from the investigations and the following further measures are recommended:-

(1) The exact sympathetic outflow to the upper extremity in man should be determined by electronic stimulation of the paravertebral ganglia, in every case operated on. This was done in case number 15. Vasoconstriction should be judged by plethysmography. The upper limit of outflow is the important factor.

(2) Similarly, by electronic stimulation, the precise sympathetic supply to the pupil and to the heart should be estimated.

(3) The reaction of the normally innervated extremity to intramuscular pilocarpine should be investigated in a further series of cases.

(4) The reaction of the sympathectomised extremity to intramuscular pilocarpine should be studied after a still further lapse of time. This applies particularly to those cases sympathectomised by removal of the second, third and fourth thoracic ganglia, and to those cases of Raynaud's Phenomena now being treated by removal of the middle cervical, stellate and second and third thoracic ganglia, (de Takats' procedure).

(5) Sudomotor and vasomotor tests should be recorded at short intervals after sympathectomy of the upper extremity by de Takats' procedure for a period of not less than three years after operation. Evaluation of

/these tests

these tests at the end of this period will give incontrovertible proof of the success or failure of this procedure for Raynaud's Phenomena of the upper extremity.

(6) Histologic examination of the sympathetic chain should be performed, where possible, in all cases of Raynaud's Phenomena re-operated on for failure of the original sympathectomy.

(7) The histology of the sympathetic chain in monkeys, after sympathectomy by removal of the second, third and fourth thoracic ganglia, should be carried out in the surviving animals after a further lapse of time. Also the histologic examination should be performed in all animals sympathectomised by ganglionectomy.

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X. ACKNOWLEDGMENTS.

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XI. BIBLIOGRAPHY.

1. Adson, A.N. and Brown, G.E.
Am. J. Med. Sc.,
1928, 170: 232.

2. Idem
Surg. Gynec. & Obst.,
1929, 47: 577.

3. Allen, A.W.
Tr. New England S. Soc.,
1932, 13: 252.

4. Allen, E.V., Barker, N.W. and Hines, F.A.
Peripheral Vascular Diseases.
Wm. Saunders & Co., Philadelphia,
1946.

5. Allen, E.V. and Brown, G.E.
Ann. Int. Med.,
1928, 1: 535.

6. Idem
J. A. M. A.,
1932, 99: 1472.

7. Idem
Am. J. Med. Sc.,
1932, 183: 187.

8. Andersen, R.C. and Gray, E.B.
Arch. Ophthalm.,
1937, 17: 662.

9. Ascroft, P.B.
Brit. J. Surg.,
1937, 24: 787.

10. Atlas, L.N.
Ann. Surg.,
1941, 114: 456.

11. Axford, D.M.
J. Anat.,
1927, 62: 301.

12. Bancroft, J.
Am. J. Physiol.,
1898, 1: 477.

13. Barron, D.H. and Matthews, B.H.C.
Am. J. Physiol.,
1935, 85: 104.

14. Bayliss, W.M.
J. Physiol.,
1901, 26: 173.

15. Beal, -.
Phil. Trans. Roy. Soc. London,
1860, 150: 611.

16. Beattie, J.
Canad. M. Ass. J.,
1932, 26: 400.

17. Bennett, T.I. and Boulton, E.D.
Am. J. Med. Sc.,
1928, 176: 657.

18. Bernard, C.
C. rend. Soc. biol.,
1851, 3: 163. and 1852, 4: 168.

19. Bichat, M.F.X.
1799. Cited by Sheehan (1936).

20. Botar, J. — Ann. Anat. path. med.-chir., 1932, 9: 449.

21. Brown, G.E. — Arch. Int. Med., 1925, 35: 56.

22. Idem — J. A. M. A., 1926, 87: 379.

23. Brown-Sequard — 1852. Cited by Sheehan (1936).

24. Bruning, F. — Klin. Wschr., 1932, 2: 777.

25. Bucy, P.C. — Arch. Neurol. & Psychiat., 1935, 33: 30.

26. Bulbring, G.E. and Burn, J.H. — J. Physiol., 1935, 83: 483.

27. Burn, J.H. — Physiol. Rev., 1938, 18: 137.

28. Idem — J. Physiol., 1922, 56: 232.

29. Idem — J. Physiol., 1925, 60: 365.

30. Capps, R.B. — J. Clin. Invest., 1936, 15: 229.

31. Carpenter, W.M. and Carpenter, E.W. — Arch. Ophthalm., 1938, 19: 111.

32. Carmichael, E.A., Honeyman, W.M., Kolb, L.C. and Stewart, W.K. — J. Physiol., 1941, 99: 329.

33. Cehanovic — 1897. Cited by Shaw (1946).

34. Clymer — 1870. Cited by Goetz (1948).

35. Cole-Rous, M. — 1948. (Unpublished data).

36. Craig, M.M. and Horton, B.T. — Surg. Clin. N. Amer., 1938, 18: 899.

37. Craig, M.M. and Kernohan, J. — Surg. Gynec. & Obst., 1933, 56: 767.

38. Cushing, H. — Proc. Nat. Acad. Soc., 1931, 17: 178.

39. Dale, H.H. and Richards, A.N. — J. Physiol., 1918, 52: 110.

40. Dastre and Morat — Cited by Sheehan (1936).

41. Davis, L. — Surg. Gynec. & Obst., 1926, 42: 729.

42. de Lorimer, A.A. — Handbook of Roentgen Diagnosis. The Year Book Publishers, Chicago, 1943.

43. de Takats, G. — Arch. Int. Med., 1937, 60: 990.

44. Idem — Am. J. Surg., 1940, 47: 78.

45. Idem — Surgery, 1947, 2: 46.

46. Deutsch, F. — J. Lab. & Clin. Med., 1941, 26: 1729.

47. Dittmar — 1870. Cited by Sheehan (1936).

48. du Petit — 1727. Cited by Sheehan (1936).

49. Ehrenberg — 1836. Cited by Sheehan (1936).

50. Elliott, T.R. — J. Physiol., 1905, 32: 401.

51. Etienne — 1545. Cited by Sheehan (1936).

52. Eulenberg, A. and Landois, L. — Virchows Arch., 1876, 66: 489.

53. Eustachio, B. — 1552. Cited by Sheehan (1936).

54. Fatheree, T.J., Adson, A.W. and Allen, E.V. — Surgery, 1940, 7: 75.

55. Fatheree, T.J. and Allen, E.V. — J. Clin. Invest., 1938, 17: 109.

56. Foerster, O. — Handbuch Neur., 1936, 5: 1.

57. Frank, F. — Cited by Bruning (1923).

58. Freeman, N.E. — Am. J. Physiol., 1935, 113: 384.

59. Freeman, N.E., Smithwick, R.H. and White, J.C. — Am. J. Physiol., 1934, 107: 529.

60. Fulton, J.F. — Physiology of the Nervous System. Oxford University Press, 1943.

61. Funaoka, S. — Far East A. Trop. Med., Tr. Seventh Congr., 1928, 1: 424.

62. Galen — Cited by Sheehan (1936).

63. Gask, G.E. and Ross, J.P. — Surgery of the Sympathetic Nervous System. (2nd Edition). W. Wood & Co., Philadelphia. 1937.

64. Gaskell, W.H. J. Physiol., 1886, 7: 1.

65. Gellhorn, A. and Steck, T. Am. Heart J., 1939, 18: 206.

66. Geohegan, W.A. and Aidar, O.J. Proc. Soc. Exper. Med. & Biol., 1942, 50: 365.

67. Geohegan, W.A. et al Am. J. Physiol., 1942, 135: 324.

68. Gibbon, J.H. and Landis, E.M. J. Clin. Invest., 1932, 11: 1019.

69. Gibson, W.C. J. Neurophysiol., 1940, 3: 237.

70. Goetz, R.H. Arch. f. d. ges. Physiol., 1935, 235: 271.

71. Idem Quart. J. Exper. Physiol., 1939, 29: 239.

72. Idem Clin. Proc., 1942, 1: 190.

73. Idem S. Afr. J. M. Sc., 1943, 8: 65.

74. Idem S. Afr. M. J., 1945, 19: 91.

75. Idem Am. Heart J., 1946, 31: 146.

76. Idem S. Afr. M. J., 1947, 21: 2.

77. Idem Lancet, 1948, 1: 830.

78. Idem Internat. Abst. Surg., 1948, 87: 417.

79. Goetz, R.H. and Cole-Rous, M. Clin. Proc., 1942, 1: 244.

80. Goetz, R.H. and Marr, J.A.S. Clin. Proc., 1944, 3: 102.

81. Goltz 1864. Cited by Sheehan (1936).

82. Gowers 1888. Cited by Sheehan (1936).

83. Grant, R.T. Clin. Sc., 1935, 11: 1.

84. Green, H.D. and Hoff, E.C. Am. J. Physiol., 1937, 118: 641.

85. Grimson, K. Surgery, 1946, 19: 277.

86. Gurney, R. and Bunnell, I.L. J. Clin. Invest., 1942, 21: 269.

87. Haimovici, H. and Hodes, R. Am. J. Physiol., 1940, 128: 463.

88. Hammond, W.S. and Yntema, C.L. J. Comp. Neurol., 1947, 87: 137.

89. Hampel, C.W. Am. J. Physiol., 1935, 111: 611.

90. Hare, K. and Geohegan, W.A. Am. J. Physiol., 1939, 126: 524.

91. Harman, N.B. J. Anat. Physiol., 1900, 34: 301.

92. Haxton, H. Brit. J. Surg., 1947 (a), 35: 69.

93. Idem Lancet, 1947 (b), 2: 598.

94. Heidenhain 1872. Cited by Sheehan (1936).

95. Heinbecker, P. and Bishop, G.H. Ann. Surg., 1938, 107: 770.

96. Heinbecker, P. Ann. Surg., 1940, 112: 1096.

97. Henle 1840. Cited by Sheehan (1936).

98. Hines, F.A. and Christensen, N.A. J.A. M. A., 1945, 129: 1.

99. Hinsey, J.C. Ann. Rev. Physiol., 1939, 1: 407.

100. Hinsey, J.C. and Gasser, H.S. Am. J. Physiol., 1930, 92: 679.

101. Hinsey, J.C. Phillips, R.A. and Hare, K. Proc. Soc. Exper. Biol. & Med., 1939, 41: 411.

102. Hirschmann 1863. Cited by Sheehan (1936).

103. Hoff, E.C. and Green, H.D. Am. J. Physiol., 1936, 117: 411.

104. Huguier 1842. Quoted by Raynaud (1862).

105. Hunt, J.H. Quart. J. Med. N. S., 1936, 5: 399.

106. Hunter, J.I. Surg. Gynec. & Obst., 1924, 39: 721.

107. Hutchinson, J. Clin. J., 1896, 7: 240.

108. Hyndman, O.R. and Wolkin, J. Arch. Neurol. & Psychiat., 1941, 46: 1006.

109. Idem Am. Heart J., 1942, 23: 535.

110. Iwai and Nin Jap. M. World, 1926, 6: 345. (Quoted by Stats and Wasserman - 1943)

111. Jaboulay, M. 1893. Cited by le Riche (1913).

112. Johnson, C.A. Surg. Gynec. & Obst., 1741, 72: 889.

113. Johnson, C.A., Scupham, G.W. and Gilbert, N.C. Surg. Gynec. & Obst., 1933, 56: 767.

114. Johnstone 1764. Cited by Sheehan (1936).

115. Jones, D.S. Anat. Rec., 1937, 70: 45.

116. Idem Anat. Rec., 1939, 73: 343.

117. Idem Anat. Rec., 1941, 79: 7.

118. Jonnesco, T. Centralbl. f. Chir., 1897, 24: 33.

119. Idem Presse Med., 1921, 1: 193.

120. Kerper, A.H. and Collier, W.D. Proc. Soc. Exper. Med. & Biol., 1927, 24: 493.

121. Kilvington, B. and Osborne, W.A. J. Physiol., 1907, 35: 460.

122. Kirgis, H.D. and Kuntz, A. Arch. Surg., 1942, 44: 95.

123. Kleinefelter, E.W. Arch. Dermat. Syph., 1936, 34: 887.

124. Kraetzer, A.F. N.Y. State J. Med., 1935, 35: 1130.

125. Kramer, J.G. and Todd, T.W. Anat. Rec., 1914, 8: 243.

126. Kuntz, A. J. Comp. Neurol., 1922, 34: 1.

127. Kuntz, A. Arch. Surg., 1927, 15: 871.

128. Kuntz, A., Alexander, W.F. and Furculo, C.L. Ann. Surg., 1938, 107. 25.

129. Kuntz, A. and Dillon, J.B. Arch. Surg., 1942, 44: 772.

130. Kure, K., Ichiko, K.I. and Ishikawa, K. Quart. J. Exper. Physiol., 1931, 21: 1.

131. Landis, E.M. Heart, 1931, 15: 247.

132. Landis, E.M. and Gibbon, J.H. Arch, Int. Med., 1933, 52: 785.

133. Langley, J.N. J. Physiol., 1895, 18: 280.

134. Idem J. Physiol., 1897, 22: 215.

135. Idem J. Physiol., 1922, 56: 110.

136. Idem J. Physiol., 1923, 58: 70.

137. Langley, J.N. and Anderson, H.K. J. Physiol., 1904, 30: 439.

138. Langley, J.N. and Dickinson, J. Proc. Roy. Soc., 1890, 47: 379.

139. Lapinski 1908. Quoted by Shaw (1946).

140. Lee, F.C. Physiol. Rev., 1929, 9: 575.

141. Legoff, J.M. Presse Med., 1933, 41: 628.

142. le Riche, R. Lyon. Chir., 1913, 10: 378.

143. le Riche, R. and Fontaine, R. Strasbourg Med., 1928, 86: 101.

144. Lewis, T. Heart, 1929, 15: 7.

145. Idem Heart, 1930, 15: 177.

146. Idem Lancet, 1931, 1: 1138.

147. Lewis, T. Clin. Sc., 1938, 3: 287.

148. Idem Brit. Med. J. 1941, 2: 795.

149. Lewis, T. and Landis, E.M. Heart, 1931, 15: 330.

150. Lewis, T. and Pickering, G.W. Heart, 1931, 15: 385.

151. Idem Heart, 1931, 16: 33.

152. Idem Clin. Sc., 1934, 1: 327.

153. Lindsley, D.B. and Sassaman, W.M. J. Neurophysiol., 1938, 1: 342.

154. List, C.F. and Peet, M.M. Arch. Neurol, & Psychiat., 1938, 39: 1228.

155. Ludwig 1851. Cited by Sheehan (1936).

156. Machida, K. Bull. Johns Hopkins Hosp., 1929, 45: 247.

157. Maxwell, S.S. Am. J. Physiol., 1902, 7: 369.

158. Meckel 1751. Cited by Sheehan (1936).

159. Meisner 1857. Cited by Sheehan (1936).

160. Meltzer, S.T. Am. J. Physiol., 1904, 11: 37.

161. Meltzer, S.T. and Meltzer, C. Am. J. Physiol., 1903, 9: 147.

162. Idem Am. J. Physiol., 1903, 9: 252.

163. Meltzer, S.T. and Auer, C.M. Am. J. Physiol., 1904, 11: 28.

164. Morton, J.J. and Scott, W.J.M. J. Clin. Invest., 1931, 9: 235.

165. Mueller, L.R. Deutsche Ztschr. f. Nervenh., 1913, 47: 413.

166. Mufson, I. Ann. Int. Med., 1944, 20: 228.

167. Muller 1838. Cited by Sheehan (1936)

168. Osler, Wm. Quoted by Langdon-Brown, W. and Evans, G. in Price's Textbook of Medicine, Oxford University Press. 1936.

169. Papez, J.W., Jensen, A.V. and Dukes, H.H. J. Neurophysiol., 1945, 8: 1.

170. Peet, M.M. and Kahn F.A. Arch. Neurol. & Psychiat., 1936, 35: 79.

171. Penfield, W. Arch. Neurol. & Psychiat., 1929, 22: 358.

172. Peters, G. Arch. f. d. ges. Physiol., 1939, 241: 201.

173. Pick, J. and Sheehan, D. J. Anat., 1946, 80: 12.

174. Pilcher, C., Wyatt, T.E. and Carney, H.M. Arch. Neurol. & Psychiat., 1941, 45: 321.

175. Pitts, R.F., Larrabee, M.G. and Bronk, D.W. Am. J. Physiol., 1941, 134: 359.

176. Potts, L.W. Anat. Anz., 1914, 13: 8.

177. Potts, T.K. J. Anat., 1925, 59: 129.

178. Pribram, B. Mir. Med. Woch., 1920, 2: 1284.

179. Pye-Smith, P.H. J. Physiol., 1887, 8: 25.

180. Racle, C. Gazette Medicale de Paris, 1859. (Quoted by Raynaud - 1862).

181. Ranson, S.W. and Billingsley, P.R. Am. J. Physiol., 1916, 41: 85.

182. Idem J. Comp. Neurol., 1918, 29: 359.

183. Ranson, S.W. and Magoun, H.W. Arch. Neurol. & Psychiat., 1933, 29: 179.

184. Ranson, S.W. and Wightman, W.D. Am. J. Physiol., 1922, 62: 392.

185. Ray, B.S., Hinsey, J.C., Hare, K. and Geohegan, W.A. Tr. Am. Neurol. Ass., 1942, 68: 51.

186. Ray, B.S., Hinsey, J.C. and Geohegan, W.A.
Ann. Surg.,
1943, 118: 647.

187. Raynaud, Maurice 1862.
"On local asphyxia and symmetrical gangrene of the extremities."
Translated by Thomas Barlow.
Selected Monographs.
The New Sydenham Society, London,
1888.

188. Reissner 1862. Cited by Sheehan (1936).

189. Remak 1838. Cited by Sheehan (1936)

190. Richter, C.P. Am. J. Physiol.,
1924, 68: 147.

191. Idem Bull. Johns Hopkins Hosp.,
1929, 45: 56.

192. Idem J. Neurosurg.,
1946, 3: 181

193. Richter, C.P. and Katz, D.I.
J. A. M. A.,
1943, 122: 648.

194. Richter, C.P. and Otanesk, F.J.
J. Neurosurg.,
1946, 3: 120.

195. Richter, C.P. and Tower, S.S.
Arch. Neurol. & Psychiat.,
1931, 26: 485.
1932, 28: 1139.
1932, 28: 1149.

196. Richter, C.P. and Whelan, F.
J. Neurophysiol.,
1943, 6: 191.

197. Richter, C.P. and Woodruff, B.G.
Tr. Am. Neurol. A.,
1942, 68: 54.

198. Richter, C.P., Woodruff, B.G. and Eaton, B.C.
J. Neurophysiol.,
1943, 6: 417.

199. Rognetta 1834. Quoted by Raynaud (1862).

200. Romanes, G.J. J. Anat.,
1946, 80: 205.

201. Ross, J.P. Brit. J. Surg.,
1935, 23: 433.

202. Roth, G.M. Surg. Clin. N. Amer.,
1938, 18: 899.

203. Sanders, A.G., Ebert, R.H. and Florey, H.W.
Quart. J. Exper. Physiol.,
1940, 30: 281.

204. Sarnoff, S.J. and Simeone, F.A.
J. Clin. Invest.,
1947, 26: 453.

205. Schiff, M. 1862. Cited by Sheehan (1946).

206. Schroeder, B. 1629. Quoted by Adson and Brown (1929).

207. Scott, E. and Palmer, D.M.
Am. J. Cancer,
1932, 16: 903.

208. Scott, W.J.M. and Morton, J.J.
J. A. M. A.,
1931, 97: 1212.

209. Semon, F. Brit. Med. J.,
1913, 1: 278.

210. Shaw, R.C. Am. J. Surg.,
1946, 71: 181.

211. Sheehan, D. Brit. J. Surg.,
1933, 20: 412.

212. Idem Arch. Neurol. & Psychiat.,
1936, 35: 1081.

213. Idem J. Comp. Neurol.,
1941, 75: 341.

214. Sheehan, D. and Marazzi, A.S.
J. Neurophysiol.,
1941, 4: 68.

215. Shinosaki, S. Folia. Anat. Japon.,
1928, 6: 599.

216. Simeone, F.A. Am. J. Physiol.,
1938, 122: 186.

217. Simeone, F.A., Cannon, W.B. and Rosenblueth, A.
Am. J. Physiol.,
1938, 122: 94.

218. Simmons, H.T. and Sheehan, D.
Lancet,
1937, 233: 788.

219. Idem Brit. J. Surg.,
1939, 21: 234.

220. Sisson 1917. Cited by Zuckerman (1938).

221. Skoog, T. Lancet,
1947, 253: 457.

222. Smithwick, R.H. Ann. Surg.,
1936, 104: 339.

223. Idem New England J. Med.,
1937, 216: 141.

224. Idem 1940, 222: 699.

225. Smithwick, R.H. Ann. Surg., 1940, 112: 1085.

226. Idem New England J. Med., 1941, 224: 329.

227. Smithwick, R.H., Freeman, N.E. and White, J.C. Arch. Surg., 1934, 29: 759.

228. Sonntag, F. Proc. Zool. Soc. London, 1923, p.65.

229. Spurling, R.G., Jelsma, F. and Rogers, J.B. Surg. Gynec. & Obst., 1932, 54: 584.

230. Stats, -. and Wasserman, -. Med., 1943, 22: 363.

231. Storup, G., Bolton, B. and Carmichael, E.A. Brain, 1935, 58: 456.

232. Stricker 1876. Cited by Sheehan (1936).

233. Telford, E.D. Brit. J. Surg., 1935, 23: 448.

234. Idem Lancet, 1938, 1: 70.

235. Thomas, A. Rev. Neurol., 1926, 1: 767.

236. Trotter, W. and Davies, H.M. J. Physiol., 1909, 38: 134.

237. Tsukaguchi, R. Quart. J. Exper. Physiol., 1916, 9: 28.

238. Tuckett, I.L. J. Physiol., 1896, 19: 267.

239. Valentin 1836. Cited by Sheehan (1936).

240. Villaret, M., Justin-Besancon, L. and Bardin, P. Arch. d. mal. du coeur, 1935, 28: 1.

241. von Bechteren 1908. Quoted by Shaw (1946).

242. von Buskirk, C. Arch. Surg., 1941, 43: 427.

243. von Cyon 1868. Cited by Sheehan (1936).

244. v. Euler, U.S. and Gaddum, J. J. Physiol., 1931, 73: 54.

245. von Kolliker 1846. Cited by Sheehan (1936).

246. Walker, A.E. Res. Publ. Ass. Nerv. Ment. Dis., 1940, 20: 400.

247. Watts, J.W. and Fulton, J.F.
New England J. Med.,
1934, 210: 883.

248. Weber, F.P.
Brit. J. Dermat.,
1913.

249. White, J.C.
J. A. M. A.,
1930, 94: 1382.

250. Idem
J. A. M. A.,
1936, 107: 350.

251. Idem
Ann. Surg.,
1940, 112: 1098.

252. Idem
Surg. Gynec. & Obst.,
1940, 71: 334.

253. Idem
Surgery,
1944, 15: 491.

254. White, J.C. and Hamlin, H.
J. Neurosurg.,
1945, 2: 402.

255. White, J.C., Okelberry, A.M. and Whitelaw, G.P.
Arch. Neurol. & Psychiat.,
1936, 36: 1251.

256. Whytt
1751. Cited by Sheehan (1936).

257. Willis
1621. Cited by Sheehan (1936).

258. Wilson, W.C.
Brain,
1934, 57: 422.

259. Woollard, H.H.
J. Anat.,
1926, 60: 345.

260. Woollard, H.H. and Norrish, R.E.
Brit. J. Surg.,
1934, 21: 83.

261. Wrete, M.
Morph. Jb.,
1935, 75: 229.

262. Idem
Zschr. mikr. anat. Forsch.
1941, 49: 317.

263. Zuckerman, S.
Trans. Zool. Soc. London,
1938, 23: 315.