TABLE I.
Calcium and Phosphorus Contents of Dentin and Humeri of Rats.

	Molar teeth dentin		Incisor teeth dentin		Humeri	
	Ca %	P %	Ca %	P %	Ca mg/cc	P mg/cc
Controls	30.24 (±0.60)	13.79 (±0.79)	26.35 (±1.08)	14.84 (±0.61)	301.9 (±37)	139.5 (±15)
Experimentals	30.23 (±0.93)	13.79 (±0.33)	25.51 (±0.84)	15.18 (±0.27)	250.9 (±17)	115.6 (±13)

been lost by the molar teeth of the experimental animals. The composition of the dentin of the incisor teeth, which had been completely reformed several times during the period of observation, was not significantly different between the two groups of animals. The numbers enclosed within parenthesis in Table I are the standard deviations of the respective means.

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Functional Reorganization Following Preganglionectomy.

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In the human, preganglionic sympathetic outflow affecting the hand is usually over the ventral roots of thoracic nerves 2 through 9.[1] Preganglionic denervation of the upper extremity in cases of Raynaud's disease has been performed frequently by sectioning the 2nd and 3rd spinal nerves, and cutting the sympathetic trunk between the 3rd and 4th thoracic ganglia, leaving T-1 intact to avoid Horner's syndrome.

Evidence has been obtained that in these cases nervous control of vasoconstriction often returns within a relatively short time.[2] This return has been ascribed to regeneration of the preganglionic fibers.

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1 Ray, B. S., Hinsey, J. C., Hare, Kendrick, and Geohegan, W. A., *Trans. Am. Neurol. Soc.*, 1942.

2 Simmons, H. T., and Sheehan, Donal, *Brit. J. Surg.*, 1939, **27**, 234.

In order to obviate or delay regeneration, section of ventral roots has been proposed as an alternative operation.

Ray[1] reports a case in which the ventral roots of T-2 through T-9 were sectioned, with subsequent evidence of complete sympathetic denervation of the hand. Reflex changes in skin resistance were abolished, and the skin temperature rose to 32°C as compared with 22°C before operation. Within 10 weeks, however, the skin resistance reflex had returned, and the skin temperature had fallen to 24°C. Novocaine block of the ulnar nerve at this time elevated the skin temperature of the 4th and 5th fingers to 29°C. While this return of nervous control may conceivably have been due to regeneration, the shortness of the interval suggests that it may have come about in some other way.

A possible explanation is that the intact preganglionic fibers of T-1 established collaterals within the stellate ganglion and/or middle cervical ganglion, to reinnervate postganglionic neurons which had been deprived of their normal preganglionic supply.

In order to investigate the possibility of such a functional reorganization, an analogous situation was created in cats. In this animal the normal outflow to the forepad is in T-4 through T-10, with an occasional small contribution from T-3.[3, 4, 5]

If, after this normal outflow were partially or entirely interrupted, it should be found that preganglionic activity to the forepad had developed in T-1 or T-2, or had increased significantly in T-3, it would indicate that such a functional reorganization had taken place.

Method. In 9 cats, under nembutal anesthesia, laminectomy was performed, and 3 to 9 ventral roots were sectioned on one side, within the range T-3 through T-11. Skin temperatures on the normal and operated sides were followed for 2 to 6 months with the Hardy radiometer. At the end of this variable period, the spinal cord was exposed by laminectomy under nembutal anesthesia. After the dura had been opened, the upper thoracic roots were prepared for stimulation by cutting the ventral and dorsal roots close to the cord, securing the distal ends with a fine silk ligature, and cutting the dura about them so that they might be elevated from adjacent tissues. Skin resistance changes were recorded on a 2-channel instrument, each channel consisting of a Wheatstone bridge, a direct-current amplifier, and a magnetically operated stylus. One channel was used

[3] Langley, J. N., *J. Physiol.*, 1894, **15**, 176.

[4] Tower, S. S., and Richter, C. P., *Arch. Neurol. and Psychiat.*, 1931, **26**, 485.

[5] Geohegan, W. A., Wolf, G. A., Jr., Aidar, O. J., Hare, Kendrick, and Hinsey, J. C., *Am. J. Physiol.*, 1942, **135**, 324.

to record from the stimulated side; the other recorded simultaneously from the contralateral side to make sure that the stimulus was not spreading to the spinal cord, or that stimulation of muscle was not causing reflex changes. A further control on stimulus spread was obtained by observing the pupils. Any pupillary response other than ipsilateral dilatation would have indicated spread of the stimulus. The recording electrodes were small zinc plates applied, over a coating of Cambridge electrode jelly, to the volar surface of the forefoot. The grounded electrode, common to both channels, was fastened to the exposed muscles of the back.

The stimulus was applied to the roots with small bipolar electrodes, and was a 60 cycle sine wave at 2 rms volts measured under load.

This method of stimulation and recording differed in no essential respect from that used previously to determine the normal outflow.[5] To insure that minor changes in technic had not altered results, several experiments were carried out on normal animals, and, in several of the operated animals, corresponding roots of the unoperated side were stimulated.

The roots stimulated, as well as those sectioned, were identified at autopsy by dissecting the nerves into the intercostal spaces.

Results. Positive responses from T-1 or T-2 or significantly large responses from T-3 were observed in 6 of the 9 animals. These, together with typical negative records from the normal side of one animal are shown in Fig. 1. In T-1, and to a lesser extent in T-2, there is often an abrupt rise and fall in resistance coincident with the beginning and end of stimulation. This is probably due to muscular movement, and may be distinguished readily from the response due to preganglionic excitation, as the latter has a latent period of about 1 second from the start of stimulation, a more gradual rise which continues after the stimulus, and a much slower return to the base line. The responses shown here have the same form as those previously observed in determining the normal outflow.[5]

Discussion and Conclusions. We conclude from these results that a functional reorganization does take place. Although we cannot be sure that it is due to the actual growth of collaterals, its effect is the same as though this were the case.

Tower and Richter[4] observed that, following section of the sympathetic trunk below T-3, nervous control of skin resistance returned within a very short time. They suggested that, in some way, roots above this level were able to take over this function, formerly mediated by the roots below. Our results may offer an explanation of their observations, and also, of the fact that preganglionic dener-

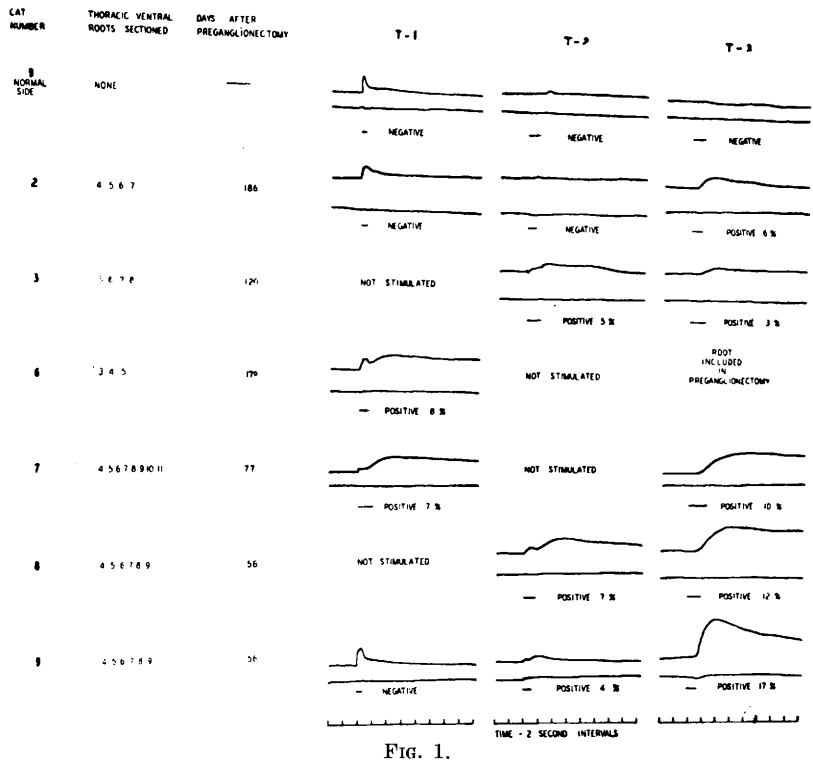

FIG. 1.

Skin resistance changes in response to ventral-root stimulation. In each record, the stimulated side is on the upper line; the contralateral side on the lower line. The short horizontal lines indicate the period of stimulation. Changes are indicated as a percentage of the basal resistance. The basal resistance varied from 6,000 to 12,000 ohms. The top and bottom sets of records are, respectively, responses to stimulation of the normal and operated sides of the same animal.

vation of the lower extremities has been generally more successful than that of the upper extremities.

It is known that return of sympathetic innervation may be brought about by actual regeneration of the preganglionic fibers.[6] Functional reorganization must also be considered in planning operations upon the sympathetic system.

Summary. Functional reorganization in the sympathetic nervous system following preganglionectomy has been demonstrated, using the cat as the experimental animal. Skin resistance change in the forepad, in response to stimulation of the ventral roots, was used as an indicator of preganglionic activity. Following interruption of preganglionic pathways to the forepad it was found that preganglionic

[6] Hinsey, Joseph C., Phillips, Robert A., and Hare, Kendrick, *Proc. Am. Physiol. Soc.*, 1939, **126**, 534.

pathways develop from roots which normally contribute nothing to the forepad.

This may offer additional explanation for early relapse following preganglionic section for Raynaud's disease in the hands, and for the fact that operations for this disease are generally more successful in the feet than in the hands.

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Quantitative Studies on Tumor Production in Mice by Benzpyrene.

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Quantitative studies on the response of animals to benzpyrene do not extend to the smallest effective doses; precise data on the effect of small amounts of other carcinogens are likewise scarce.

Brock, Duckrey and Hamperl[1] inserted a collodion sac containing crystals of 3-4 benzpyrene (500 to 25,000 γ) into the peritoneum of rats. They estimated that about 1 γ of benzpyrene passed the collodion membrane daily; this was sufficient to induce sarcoma in the majority of animals. Oberling and M. and P. Guérin[2] obtained sarcomata in 4 of 35 rats that had received a single subcutaneous injection of 100 γ of benzpyrene in olive oil and in 1 of 10 rats injected with 50 γ of benzpyrene. Shimkin and Andervont[3] injected male mice of C_3H stock with 0.2 cc of tricaprylin containing from 250 to 2000 γ of benzpyrene. All animals developed tumors after injection of 2000 and 1000 γ; 19 of 20 and 18 of 20, respectively, were positive after injection of 500 γ and 250 γ. The same amounts of benzpyrene were injected into hybrid mice, but the results were more irregular, and tumors failed to appear in at least one-third of the injected animals. Bryan and Shimkin,[4] analyzing the values of latent period of tumors obtained by the former authors in C_3H mice (87 to

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† These experiments were performed in the Department of Pathology of the University of Liége from November, 1938, to May, 1940.

1 Brock, N., Duckrey, H., and Hamperl, H., *Arch. f. exp. Path. u. Pharmakol.*, 1938, **189**, 709; *Arch. f. klin. Chirurg.*, 1938, **194**, 250.

2 Oberling, Ch., Guérin, M. and P., *Bull. Assn. Fr. Etude Canc.*, 1939, **28**, 198.

3 Shimkin, M. B., and Andervont, H. B., *J. Nat. Canc. Inst.*, 1940, **1**, 57.

4 Bryan, W. R., and Shimkin, M. B., *J. Nat. Canc. Inst.*, 1941, **1**, 807.