THE UNION OF DIFFERENT KINDS OF NERVE FIBRES.

BY J. N. LANGLEY, F.R.S., AND H. K. ANDERSON, M.D.

(From the Physiological Laboratory, Cambridge.)

CONTENTS.

Introduction. Flourens in 1828[1] was apparently the first to try whether the central end of one nerve could make functional union with the peripheral end of another. His well-known observations on the fowl proved that this was the case for the two main nerves proceeding from the brachial plexus.

Observations of a similar nature have been made on the mammal[2] by Rawa, Stefani, Howell and Huber, Cunningham, Forsmann, Kennedy and Bethe, with similar results. It has moreover been shown that the central end of the spinal accessory nerve can make functional union with the peripheral end of the facial[3].

[1] Flourens. *Ann. des Sci. Naturelles*, III. p. 113. 1828.

[2] Rawa. *Arch. f. (Anat. u.) Physiol.* 1885, p. 296.
Stefani. *Arch. f. (Anat. u.) Physiol.* 1886, p. 488.
Howell and Huber. This *Journal*, XIII. p. 335. 1892.
Cunningham. *Amer. Journ. Physiol.* I. p. 239. 1898.
Forsmann. *Ziegler's Beiträge*, XXVII. pp. 212, 231. 1900.
Kennedy. *Phil. Trans. Roy. Soc.* B. 194, p. 127. 1901 (Read Nov. 1900).
Bethe. *Allgemeine Anat. u. Physiol. des Nervensystems*, Leipzig, 1903, p. 182 et seq.

[3] This operation was first performed by Ballance. See also Kennedy, *op. cit. supra*; Breàvoine, *Chipaults' Travaux de Neurol. Chirurg.* 6me Ann. p. 92; Ballance and Purves Stewart, *Brit. Med. Journ.* May 2, 1903; Cushing, *Journ. Nervous and Mental Diseases*, 1903, p. 367.

The results establish a probability that the central end of any nerve supplying skeletal muscle or skin can make functional connection with the peripheral end of any other similar nerve.

Observations of an allied kind[1] were made by Philipeaux and Vulpian, by Schiff and Reichert and by Rawa. They joined the central end of the vagus to the peripheral end of the hypoglossal nerve, and found that the vagus acquired a certain degree of motor effect on the muscles of the tongue. Since the vagus contains efferent fibres for striated muscle, the result may be taken as a further instance of the power of cross union of the efferent fibres of striated muscle.

A different line of research was started by an experiment of Schwann's[2]. He cut the sciatic nerve in a frog, and after an interval stimulated the peripheral ends of the anterior and posterior roots of the nerves making up the sciatic. He found that though contraction of the muscles of the lower leg was obtained by stimulating the anterior roots, no contraction was obtained by stimulating the posterior roots; showing that the afferent fibres in the sciatic had not united with the efferent fibres. Steinrück[3] made a similar experiment with the same result. In the mammal a similar experiment was made by Schiff[4]. He cut the brachial nerves in a dog, and 14 months later, when movement and sensation had returned to the fore-limb, stimulated the anterior and posterior roots of the nerves. The peripheral end of the posterior roots gave no effect.

Other experiments on the union of roots and sensory fibres were initiated by Bidder[5], who attempted a cross union of the hypoglossal and lingual nerves. Experiments on the same lines[5] were made by

[1] Philipeaux and Vulpian, *Journ. de la Physiol.* VI. p. 427, 1863. Schiff and Reichert; Schiff, *Arch. des Sci. phys. et nat.* 1885 (Gesam. Abh. I. p. 729); Reichert, *Amer. Journ. Med. Sci.* N.S. 89, p. 146, 1885; Rawa, *op. cit. supra.* Ballance and Purves Stewart (*op. cit.*) quote Barrago-Ciarella as having successfully joined the vagus to the facial.

[2] Schwann. *Müller's Physiol.* 3te Aufl. I. p. 415.

[3] Steinrück, quoted from Bidder, *Müller's Arch.* 1842, p. 107.

[4] Schiff. Gesamm. Abhandl. I. p. 724.

[5] Bidder. *Müller's Arch.* 1842, p. 102.
Schiff. *Lehrb. d. Physiol.* Lahr. I. p. 133. 1858—59.
Gluge and Thiernesse. *Journ. de la Physiol.* II. p. 686. 1859.
Philipeaux and Vulpian. *Journ. de la Physiol.* VI. pp. 421, 474. 1863.
Vulpian. *Leçons sur la Physiol. gén. et comp. du Système Nerveux*, p. 276. Paris, 1866 (quoted from *Hermann's Hand.* II. Th. 1. p. 11).
Rosenthal. *Centralb. f. d. med. Wiss.* 1864, p. 449 (quoted from Bidder, *op. cit. infra*, p. 296).
Bidder. *Arch. f. Anat. u. Physiol.* 1865, p. 246.

Schiff, Gluge and Thiernesse, Philipeaux and Vulpian, Vulpian, Rosenthal and again by Bidder.

Vulpian's later experiments[1] went far towards proving that such motor effect as was obtained in the tongue when the central end of the lingual was joined to the peripheral end of the hypoglossal, was due to the chorda tympani fibres in it, and that the sensory fibres did not make functional union with the motor fibres. With regard to the union of central motor fibres to peripheral sensory, the experiments are not of a nature to give any result, since stimuli do not pass back through motor nerve cells. A new line of investigation is here required, viz. the examination of the nerve-endings after time has been allowed for regeneration, to see whether they are of the normal sensory type.

It will be noticed that in the foregoing cases in which cross union was effective both central and peripheral ends of the nerves contained efferent nerve fibres supplying multinuclear striated muscle. An experiment of a different order was made by Rawa (*op. cit. supra*) though he did not himself regard it as such. He joined the central end of the hypoglossal to the peripheral end of the vagus[2], and found that the hypoglossal acquired some inhibitory power on the heart beat; the experiments are not entirely conclusive, since it is not clear that fibres may not have grown down from the central end of the vagus, and have been stimulated with the hypoglossal fibres.

The observations of one of us on the sympathetic system led to a more definite knowledge with regard to two other classes of efferent fibres, viz. pre-ganglionic fibres arising in the spinal cord and ending in the sympathetic ganglia and post-ganglionic fibres arising in the sympathetic ganglia and ending in the tissues. It was natural then to make observations on the cross union of these. It was shown that pre-ganglionic fibres of different kinds could unite with one another and that post-ganglionic fibres of different kinds could unite with one another[3]. Moreover it was found that pre-ganglionic fibres of cranial nerves (the vagus and chorda tympani) could unite with the pre-ganglionic fibres of the cervical sympathetic[4]. By the nicotine method it was shown that the vagus fibres which had united with the pre-ganglionic fibres had become connected with the nerve cells of the

[1] Vulpian. *Arch. de Physiol. norm. et path.* 1873, p. 597. Cp. also 1874, p. 704.

[2] Flourens (*op. cit. supra*) joined the central end of the 5th cervical nerve to the peripheral end of the vagus, but did not find any sign of union between them.

[3] Langley. This *Journal*, XXII. p. 215. 1897.

[4] Langley. This *Journal*, XXIII. p. 240. 1898.

superior cervical ganglion. And it appeared from the one experiment made that pre-ganglionic fibres could not make functional union with post-ganglionic fibres[1].

Recently a considerable number of experiments on the cross union of nerve fibres of various kinds have been made by ourselves and by others. In this Paper we propose to consider what general rules can be deduced from them.

Nomenclature. We use the term 'somatic nerves' in the usual and convenient, though inaccurate, manner to include (*a*) the efferent nerve fibres which arise in the brain and spinal cord and which have no nerve cells in their course and (*b*) the efferent fibres which arise from the spinal ganglia and from the similar cranial ganglia.

We speak of two nerves as being 'functionally united' without prejudice to the question of the method by which the function is acquired, whether by histological union of the nerve fibres (the coalescence theory) or by down growth of the central axis cylinders (the out-growth theory). If the latter theory is true, the term functional union represents only the anatomical and physiological condition; if the former theory is true, the term represents also the histological condition.

In the case of efferent nerves, we speak of a central end as being functionally united to a peripheral end, when electrical stimulation above and below the point of junction causes some peripheral motor effect. This implies that the peripheral end of the nerve including nerve-endings of some sort have regenerated, that there is continuity between the central and peripheral end, and that nervous impulses can pass from the central nervous system to the peripheral tissue. The term 'functional union' is sometimes used to mean more than this, viz. that the possible path from the central nervous system is in fact used, and in a normal manner. That is however a separate question[2].

We shall have little occasion to speak of the functional union of two afferent nerves, but when we do, we mean not simply that electrical stimulation of the peripheral end can give rise to a reflex, but also that the sensory nerve-endings have regrown, and are capable of transmitting impulses.

In discussing such union as may take place between motor and sensory nerves and *vice versâ*, the term functional union is best avoided,

[1] Langley. This *Journal*, xxv. p. 417. 1900.

[2] In the abstracts of the experiments, we give for future reference, such signs as we have noticed of the use of a united nerve by the central nervous system.

for in some of the conceivable unions there can hardly in the nature of the case be any function; thus if a motor nerve fibre were to unite with a sensory nerve fibre, an impulse set up in the united nerve would be unable to pass back through the nerve cell and probably unable to pass outward from the nerve-endings.

Animals and anæsthetics. Our experiments have been made on cats and on two rabbits. In the preliminary operation of section and union of the nerves, ether was used as an anæsthetic; the operation was performed with antiseptic precautions and the wounds healed by first intention. During the final examination, chloroform was first given and then A.C.E. mixture by a tracheal tube.

Abbreviations in the abstracts of the experiments. In the abstracts of the experiments when a nerve is said to cause an effect, it means that the effect was produced by electrical stimulation of the nerve; the electrical stimulation employed was the interrupted current of a du Bois Reymond induction machine, the shocks being distinctly but not strongly felt when the electrodes were placed on the tip of the tongue. As a rule the nerves were stimulated a number of times, the strength of the shocks varying from weak to strong.

In speaking of the union of the central end of one nerve with the peripheral end of another, we put first the nerve the central end of which was taken; thus union of the spinal accessory nerve with the cervical sympathetic means union of the central end of the former with the peripheral end of the latter.

1. THE UNION OF SOMATIC NERVE FIBRES WITH ONE ANOTHER.

Previous observations—briefly mentioned in the Introduction—have given such uniform results with regard to the union of the central end of one nerve supplying skeletal muscle with the peripheral end of another similar nerve, that we have not thought it necessary to make any further experiments on the point.

Our experiments have dealt chiefly with the union of central end with central end, and of peripheral end with peripheral end of two nerves. A short statement of the results obtained, was communicated to the Physiological Society in Dec. 1902[1]. The attempt to join the central ends of two nerves was first made by Schiff[2]. After allowing

[1] *Proc. Physiol. Soc.* p. iii. (This *Journal*, XXIX. 1903).
[2] Schiff. *Lehrb. d. Physiol.*, Lahr. p. 136. 1858—59.

time for regeneration one of the nerves was cut near its origin, and the end connected with the neurome stimulated. No reflex was obtained until the nerve was stimulated close to the neurome. Similar experiments, with the same results have been made by Stefani[1], by ourselves (cp. Exps. 1 and 2 below) and by Bethe[2]. Bethe varied the form of the experiment by connecting the central end of the sciatic of one side with the central end of the sciatic of the opposite side.

All the observations then agree that the central afferent fibres of one nerve neither unite with the central afferent fibres of another nerve, nor do the afferent fibres of the one grow out to any considerable extent amongst the fibres of the other.

On the union of the peripheral ends of two nerves we have made four experiments. Exp. 1 was made on a rabbit. The internal and external popliteal nerves were taken for several reasons; both contain efferent as well as afferent fibres, they are branches of the same nerve, and many of the afferent fibres would be frequently stimulated by contact of the foot with the ground. 124 days were allowed for regeneration and union. The central ends of the nerves had not formed any functional connection with the peripheral ends so that there was no complication on this account. The peripheral ends were joined by a swelling but no trace of effect was obtained by stimulating either of them, either directly or reflexly. Thus the peripheral ends had not made any functional connection with one another. It may be noticed that the nerves were frequently excited mechanically by the walking and running movements of the animal and that this excitation did not prevent the loss, or cause the return, of excitability in the nerves.

Union of two mixed nerves (a) central end to central end, and (b) peripheral end to peripheral end.

Exp. 1. Rabbit. The internal and external popliteal nerves were cut on the left side in the upper part of the thigh; the two central ends were sewn together, and the two peripheral ends were sewn together.

124 *days later*. The left posterior tibial nerve exposed at the ankle caused no body movement nor change in respiration, nor movement of the foot. The (original) peripheral portions of the internal and external popliteal nerves were also without effect either on electrical stimulation, crimping, application of ammonia, and of 1 p.c. nicotine.

The central portions of the internal and external popliteal nerves were then examined. The external popliteal was separated from the internal above the neurome and cut about 3 cm. centrally of it. The end connected with the neurome gave no reflex effect either on

[1] Stefani. *Arch. f. (Anat. u.) Physiol.* 1886, p. 488.
[2] Bethe. *Anat. u. Physiol. d. Nervensystems*, Leipzig, 1903, p. 220.

the muscles or on respiration except when the electrodes nearly touched the neurome ; on stimulating the neurome there was at once reflex body movement.

The internal popliteal nerve was also cut, neither this nor the external popliteal had any effect on the foot, *i.e.* no connection had been established between the central and peripheral portions of the nerves.

The experiment was repeated in a modified form in a kitten[1]. The peripheral ends of the external and internal popliteal nerves were sewn together and 205 days allowed for union to take place, then the tissue a short distance from the neurome was cut through to cause degeneration in any fibres which might run to the nerves from the central nervous system. Forty-two days after this the nerves were stimulated. The stimulation was without any observable effect, *i.e.* no union had taken place between the peripheral ends of the nerves.

A further experiment (Exp. 2 below) gave a different result and seemed at first sight opposed to the conclusion drawn from the first two.

Union of (a) central end to central end, (b) peripheral end to peripheral end of a mixed muscular nerve and of an afferent cutaneous nerve.

Exp. 2. Cat, adult, large. The internal saphenous nerve and the main muscular branch of the crural nerve were exposed below Poupart's ligament. The muscle nerve was cut near its entry into the muscles, the internal saphenous nerve was cut about a centimetre higher up. The central end of the muscle branch was turned forward and sewn to the central end of the internal saphenous nerve. The peripheral end of the internal saphenous was turned back and sewn to the peripheral end of the muscle nerve. The two loops were about a centimetre distant from one another.

67 *days later*. The internal saphenous nerve was isolated from surrounding tissue a little above the knee. Stimulation of it caused a contraction in the thigh in the region of distribution of the muscle branch, but no other reflex was observed. A small piece of the peripheral end of the nerve was cut out; it contained a considerable number of sound medullated fibres.

5 *days later*. The internal saphenous nerve was stimulated below the neurome, it produced the same effect as before.

The muscle branch was separated from the rest of the crural nerve and cut above Poupart's ligament and the end attached to the central end of the internal saphenous nerve stimulated, it caused extension of the leg but had no reflex effect.

The tissue around the junction of the peripheral end of the internal saphenous nerve and the muscle branch of the crural was cut through, stimulation of the internal saphenous nerve caused contraction of the thigh muscles as before, but much weaker. The central muscle branch stimulated near its junction with the central end of the internal saphenous had now no effect; stimulation of the central end of the internal saphenous caused a reflex body movement.

No fibres of recent degeneration were present in the nerves connected with the two neuromes ; but in the internal saphenous nerve peripherally of the spot cut in the second operation all the medullated fibres were in a stage of recent degeneration.

[1] An abstract of this experiment we shall give in a later Paper on autogenic regeneration.

The peripheral end of the muscular branch contained absolutely and relatively many more medullated fibres than the peripheral end of the internal saphenous which was joined to it.

The neurome on the central ends contained numerous interlacing medullated fibres from the two nerves.

In this case two branches of the crural nerve were taken, one the main muscular branch to the muscles of the thigh, the other the internal saphenous—a purely afferent nerve except for post-ganglionic sympathetic fibres. The two central ends were joined together and the two peripheral ends were similarly joined. 72 days were allowed for regeneration.

The peripheral part of the internal saphenous nerve caused contraction in some of the thigh muscles supplied by the peripheral end of the muscle nerve, and it did this after severance of the conjoined nerve from the central nervous system. But while the connections of the nerves were still intact, the central end of the muscle nerve was cut and its lower portion was stimulated; it was found that it had made considerable functional connection with its own peripheral end. Microscopically medullated fibres were traced from it to the internal saphenous nerve.

The latter facts suggested that the contraction produced by the internal saphenous nerve was due to its connection with the central and not to a direct connection with the peripheral end of the muscle nerve. And that this was the case Exp. 3 gives evidence.

Union of the central end of a muscular nerve with the peripheral end of a skin nerve. Axon reflex obtained.

Exp. 3. Cat, half-grown. The central end of the main muscle branch of the crural nerve was sewn to the peripheral end of the internal saphenous nerve. The end of the muscle branch was left projecting from the muscle rather less than a centimetre from the junction.

72 *days later.* Stimulation of the internal saphenous at the knee caused contraction of the thigh muscles and extension of the leg. It did not produce so far as was seen any other movement. The muscle branch of the crural was found to be united with its peripheral end as well as with the internal saphenous nerve. Section of the crural and obturator nerves centrally of Poupart's ligament did not affect the extension of the leg caused by stimulating the internal saphenous. The same movement but stronger was obtained by stimulating the muscle branch itself both centrally and peripherally. The internal saphenous was cut at the knee, stimulation of the upper end gave the effect as before, stimulation of the lower end was without effect.

Here the main muscle branch of the crural nerve was sewn to the peripheral end of the internal saphenous nerve, a portion of the central end of the saphenous was excised, and the peripheral end of the muscle nerve was left projecting from the muscle. 72 days were allowed for regeneration. The internal saphenous as in Exp. 2 caused contraction in some of the thigh muscles after section of the crural and obturator nerves near their origin, and the action was unaltered when the internal saphenous was isolated up to the neurome, *i.e.* when any direct connection which it might have made with the peripheral end of the muscle nerve was severed. As in Exp. 2 it was found that some fibres from the central end of the muscle nerve had joined the peripheral end.

The 'reflex' contraction produced by the internal saphenous nerve after severance of all connection with the central nervous system we attribute to the stimulation of nerve fibres one branch of which was in the internal saphenous and the other in the muscle nerve, *i.e.* we consider that the 'reflex' was an axon reflex.

The fibres which grow out from the central end of a nerve we know may divide, and there is nothing unreasonable in supposing that one branch of some of the nerve fibres had joined the muscle nerve and that the other branch had joined the internal saphenous nerve. In such case it follows either (*a*) that the efferent fibres of the muscle nerves had united with the (embryonic) afferent fibres of the internal saphenous nerve, which appears to us against the trend of other evidence, or (*b*) that the central efferent fibres had grown more than 7 centimetres down the sensory nerve, a fact which would be distinctly in favour of the view that regeneration consists in a growth of axis cylinders from the central end of the cut nerve.

Observations of a similar nature but on mixed nerves have been made by Bethe (*op. cit.* 1903, p. 224) and in many respects with the same results. Thus in some cases he found that the peripheral ends of the nerves had no effect on the muscles, in others he obtained a reflex similar in general to that we have described.

He attributes it however to a direct union of the peripheral nerve fibres, inclining to think that the afferent fibres of one branch had made connection with a large number of efferent fibres in the other branch. The point of view we have given above is not considered by Bethe; probably since he considered that no connection had been established between the central nervous system and the peripheral ends of the nerves. This he took to be the case mainly because he obtained no body reflex on stimulating the peripheral nerves; the evidence we think is hardly decisive, at any rate there was an absence of such reflex in our cases[1] although a central connection had certainly been established.

[1] In our experiments the animals were anæsthetized.

Bethe has shown that a nerve can be artificially lengthened. He united the sciatic of one side with the sciatic of the opposite side, and after allowing time for regeneration, stimulated the central portion of the united nerve and obtained contraction in the lower limb of the opposite side.

We made a similar experiment in 1902, but on crossed nerves. The sciatic was cut in a rabbit, the peripheral end carried through the muscles of the thigh and sewn to the chief muscle branch of the crural nerve. After 398 days, the crural nerve was stimulated, and found to cause contraction in the upper part of the gastrocnemius. The normal muscular fibres of the crural are not long enough to reach the gastrocnemius, and we conclude—as Bethe does—that short fibres are able to make functional connection with long ones[1].

The relative ease of union of long with short, and of short with long fibres deserves further investigation in view of the importance of the question in surgical cross union.

Another point we experimented on was the union of afferent with efferent fibres. In a rabbit a few days old the central end of the internal saphenous nerve was sewn to the peripheral end of the sciatic, the latter nerve being taken through the muscles of the thigh to effect the junction. 403 days later, the sciatic was cut centrally of the first point of section, and the peripheral end (with the internal saphenous nerve connected with it) stimulated, it caused reflex body movement, but no contraction in the muscles supplied by the sciatic nerve; reflex was also obtainable from the posterior tibial nerve at the ankle. Thus the afferent nerve fibres of the internal saphenous nerve had 'united' with the afferent but not with the efferent fibres of the sciatic.

2. The union of somatic efferent nerves with pre-ganglionic nerves.

Calugareanu and Henri[2] sutured the central end of the hypoglossal nerve to the peripheral end of the vagus in dogs and found in two experiments, in which 99 and 170 days respectively were allowed for regeneration, that the peripheral end of the vagus caused slowing of the heart-beat. The observations are unfortunately inconclusive since it

[1] For similar results with pre-ganglionic fibres cf. below, Exp. 10.

[2] Calugareanu and Henri. *Journ. de Physiol. et de path. gen.* 1900, p. 709. The central vagus was also joined to the peripheral hypoglossal; stimulation of the peripheral hypoglossal caused contraction in the muscles of the tongue.

was not shown that some fibres from the central end of the vagus had not rejoined the peripheral end of the nerve, and so produced the effect.

The same authors[1] have described an experiment in a dog in which the hypoglossal was joined to the chordo-lingual nerve and the animal was observed for about two years. They found after a time that feeding the animal caused a much more copious secretion from the sub-maxillary gland on the sutured side, and that stimulation of the hypoglossal nerve itself caused secretion from the gland.

We have in a former paper[2], given an account of two experiments in which the 5th cervical nerve was joined to the cervical sympathetic and in which stimulation of the 5th cervical roots caused to a greater or less degree the effects normally produced by the cervical sympathetic.

We find also that the phrenic nerve is able to unite with the cervical sympathetic and give sympathetic effects. The effects in this case were slight only, probably in consequence of the considerable reunion of the two ends of the cervical sympathetic. No movement of the nictitating membrane, eyelids or iris, which could be referred to the action of the phrenic, were however observed during life. In the abstract of this experiment we mention some points which we shall refer to later.

Cross union of phrenic and cervical sympathetic.

Exp. 4. Cat. Left side :—the root of the phrenic arising from the 5th cervical nerve was sewn to the peripheral end of the cervical sympathetic, and the central end of the cerv. symp. was sewn to the peripheral end of the cut root of the phrenic at the level of the 1st rib. Right side :—the lower half of the cerv. symp. was excised.

The paralytic effects were equal on the two sides of the head for about two months; they then gradually diminished on the left side. At no time was any change observable in the nictitating membrane, eyelids or pupil in correspondence with respiration.

197 *days later.* The nictitating membrane projected farther, the eyelids were closer, the pupil smaller, and the vessels of the ear larger on the right side than on the left.

The central end of the left vagus caused as a rule rather more retraction of the nictitating membrane, and occasionally more dilatation of the pupil on the left side than on the right.

The left cerv. symp. caused the usual sympathetic effects.

The right cerv. symp. (stimulated about 1·5 cm. below the sup. cerv. gang.) gave no effect.

Clamping the trachea tubes for 90 seconds had a rather greater effect on the nictitating membrane and pupil on the left side than on the right (the nict. memb. was first more projected, later fully retracted).

The nerve-roots after removal of the corresponding portion of the spinal cord gave the following effects:

[1] Calugareanu and Henri. *Comptes Rendus Soc. de Biol.* 1901, p. 1099.

[2] Langley and Anderson. This *Journal*, xxx. p. 439. 1904.

	Eye	Diaphragm of left side
IV. C.	0	0
V. C.	Nict. memb. and eyelids, moderate; pupil, slight	Contraction, chiefly of central part
VI. C.	0	Contraction, all parts
VII. C.	0	Contraction, all parts
VIII. C.	0	0
I. Th.	Nict. memb., slight; eyelids, very slight; pupil, moderate to good	Contraction of small ventral part
II. Th.	Nict. memb., good; eyelids and pupil moderate to good	Contraction of small part, a little more dorsal than that of I. Th.
III. Th.	Nict. memb., moderate, < I. Th.; eyelids and pupil, slight	Slight contraction of small part, a little more dorsal than that of I. Th.
IV. Th.	0	0

The contraction of the diaphragm on stimulating the thoracic nerves was a brief but fairly strong twitch; the muscle relaxing during the stimulation.

After cutting the left phrenic nerve, the spinal nerves on the left side had no effect on the diaphragm.

On dissection, the distance between the neuromes was rather more than a centimetre. Thus the central ends of the cut nerve had made better connection with their own peripheral ends across a centimetre of tissue than they had with the nerves to which they were sewn.

3. The union of pre-ganglionic nerves with somatic efferent nerves.

Mislavski[1] sewed the cervical sympathetic to the recurrent laryngeal nerve in a cat, and found after not less than 82 days that stimulation of the cervical sympathetic caused movements of the vocal cord on the same side[2]. The movements were also obtained reflexly by stimulating sensory nerves.

We have made three experiments which confirm the result obtained by Mislavski and add some facts to his account.

Contraction of the thyro-arytenoid m. continues during the period of stimulation of the normal recurrent laryngeal (interrupted current)

[1] Mislavski. *Comptes Rendus Soc. de Biol.* Paris, 1902, p. 841.

[2] In an experiment made some years ago (This *Journal*, xxiii. p. 242, 1898, Exp. 1) in which the cervical sympathetic was joined to the vagus (123 days) I noticed that the peripheral end of the vagus, though having no effect upon the œsophagus or heart, caused contraction in the crico-thyroid space. At the time it seemed possible that the result was due to a re-growth of some fibres from the central end of the vagus, and it was left over for further investigation. In the light of Mislavski's experiments and of those given in this Paper, the probability is that the contraction was really due to sympathetic fibres which had made their way along the whole length of the recurrent laryngeal. (J. N. L.)

provided it is not too long, and relaxes at once on cessation of the stimulus.

It will be seen from Exp. 5 that the cervical sympathetic and the recurrent laryngeal nerve connected with it did not produce a normal effect upon the thyro-arytenoid muscle, the contraction though strong gave way almost at once to partial relaxation. The complete relaxation after cessation of the stimulus was much slower than with the normal recurrent laryngeal. The conjoined cervical sympathetic and recurrent laryngeal also gave contraction of the arytenoideus m. but the contraction was limited to the portion on the same side, whereas the recurrent laryngeal on the other side caused strong contraction of the whole muscle.

Union of the cervical sympathetic with the recurrent laryngeal.

Exp. 5. Kitten. Right recurrent laryngeal cut about two cm. below the larynx, the peripheral end turned outwards and sewn to the central end of the cervical sympathetic. About a cm. of the peripheral part of the cervical sympathetic excised.

180 *days later.* The rt. cerv. symp. stimulated near the thorax caused movement in the crico-thyroid space (it caused also slight movement of the nictitating membrane and eyelids but no dilatation of the pupil).

The vagus was cut near the ganglion of the trunk, its peripheral end caused contraction of the œsophagus but no movement in the crico-thyroid space.

The tissue round the point of union of the cerv. symp. and recurrent laryngeal was cut through, and the external muscles of the larynx exposed; stimulation of the cerv. symp. caused no movement except in the crico-thyroid space.

The trachea was cut through just below the larynx; stimulation of the rt. cerv. symp. caused quick contraction of the right thyro-arytenoid muscle, this at once gave way to partial relaxation; on cessation of the stimulus, the complete relaxation was much slower than when the left recurrent laryngeal nerve was stimulated; the latter nerve caused quick tetanic contraction of the left thyro-arytenoid muscle. The rt. recurrent laryngeal gave the same effect as the symp. but rather more strongly. Neither rt. nor left recurrent laryngeal caused appreciable pallor of the mucous membrane.

1·5 c.c. of 1 p.c. curari was injected in the femoral vein; the action of the rt. recurrent laryngeal and rt. cerv. symp. was much more slowly abolished than that of the left recurrent laryngeal.

The rt. recurrent laryngeal (which had been joined to the cerv. symp.) contained many small medullated fibres, and 12 rather large fibres, the latter probably came from the superior laryngeal.

The thyro-arytenoid muscle was treated with gold chloride (Ranvier's boiled formic acid and gold method). Numerous motor nerve endings were found on the left side, but none on the right.

In a second experiment, after the cervical sympathetic had been joined to the recurrent laryngeal nerve, and had acquired a motor action on the thyro-arytenoid muscle, the tissue around the neurome was cut through in order to sever any nerve fibres, except sympathetic fibres, running to it. Seven days later, the cervical sympathetic and the laryngeal had the same effect as before, and there were no degenerated fibres in the joined nerves. Hence the effect was not due to any nerve fibres, except sympathetic fibres growing in at the neurome.

In order to determine whether the small medullated nerve fibres in the recurrent laryngeal after its union with the sympathetic are in trophic connection with the sympathetic fibres, the cervical sympathetic was cut (Exp. 6), after it had acquired a motor action on the thyro-arytenoid m. The experiment showed that this trophic connection existed, and that degenerative section of the cervical sympathetic abolished the motor effect of the recurrent laryngeal with which it was connected.

Union of cervical sympathetic with recurrent laryngeal; section of sympathetic 7 days before death.

Exp. 6. Cat. Central end of cerv. symp. sewn to peripheral end of recurrent laryngeal in middle of neck; peripheral end of cerv. symp. nearly as far as the sup. cerv. ganglion excised.

138 *days later.* The rt. cerv. symp. was cut low in the neck. The peripheral end caused marked movement in the crico-thyroid space on the right side, and no effect on the eye.

7 *days later.* The rt. cerv. symp. and the recurrent laryngeal nerve connected with it caused no contraction of the thyro-arytenoid muscle, nor any other effect.

The right recurrent laryngeal from its junction with the cerv. symp. onwards contained many fibres of recent degeneration, nearly all were 2 to 3·5 μ in diameter. Near the thyro-arytenoid muscle no sound fibres were present.

Five sound medullated fibres ran from the superior laryngeal downwards in the recurrent laryngeal. Two nerve filaments one containing 4, and the other 10 sound fibres also joined the recurrent laryngeal and ran downwards in it; at the junction with the cerv. symp. 20 sound fibres were present.

It may be noticed as an instance of the re-growth of the sympathetic, that a filament containing degenerated fibres ran from the sympathetic laryngeal neurome upwards alongside the vagus, and that there were 3 or 4 degenerated fibres in the sympathetic just below the sup. cerv. ganglion.

The sterno-mastoid and trapezius muscles belong to a class of muscles differing from that of the thyro-arytenoid. Moreover the nerves which run to them arise from cells in the cervical spinal cord, part of the fibres passing by way of the upper cervical nerves and part by way of the spinal accessory, whilst the nerve fibres supplying the thyro-arytenoid arise from nerve cells in the spinal bulb. Since the nerve fibres of the spinal accessory are large nerve fibres (9 to 15 μ in diameter) there was additional interest in joining the small nerve fibres of the cervical sympathetic to them. This we did in a cat (Exp. 7), and found after 175 days that the cervical sympathetic caused contraction of the sterno-mastoid though not of the trapezius. In order to avoid any question of escape of current or of the production of an axon reflex, the spinal nerves from the 8th cervical to the 6th thoracic were tied and cut in the vertebral canal and the peripheral ends stimulated. Prompt contraction of some part or other of the sterno-mastoid muscle was obtained from each of the first four thoracic nerves, the order in extent of contraction obtained being 2nd Th., 3rd Th., 1st Th., 4th Th., which is, so far as the experiments go, the order of the number of fibres the nerves respectively send to the cervical sympathetic. In this experiment the central end of the spinal accessory had united little or not at all with the peripheral end of the sympathetic, although the central end of the sympathetic had united with the peripheral end of the spinal accessory; the fact suggests that one of the factors determining the union of nerves is the relative size of the fibres in the central and peripheral ends, and that small nerve fibres can much more readily unite with large ones than large ones with small.

Union of the cervical sympathetic with the spinal accessory.

Exp. 7. Cat. Central end of rt. cerv. symp. sewn to peripheral end of the spinal accessory about a centimetre below the sup. cerv. gang. Central end of spinal accessory sewn to peripheral end of the cerv. symp. near the sup. cerv. ganglion.

175 *days later*. The vagus was tied and cut about the middle of the neck and dissected from the cerv. symp. to the lower part of the neck. The cerv. symp. was isolated from the surrounding tissue. By pulling up the vagus ligature, the cerv. symp. was slightly raised and so could be stimulated without escape to the surrounding tissue. Stimulation of the symp. with interrupted shocks not felt on the tip of the tongue caused contraction of the sterno-mastoid muscle, but not of the trapezius (it caused also slight retraction of the nictitating membrane and a trace of dilatation of the pupil).

Stimulation of the peripheral ends of the 8th C., the 5th and 6th thoracic nerves in the vertebral canal had no effect on the sterno-mastoid. The 1st thoracic caused contraction in a strip in the lower third of muscle; the 2nd thoracic caused contraction of a band stretching from one end to the other of the muscle, but not including all its fibres especially at the dorsal border; the 3rd thoracic caused contraction in the middle part of the lower half of the muscle; the 4th thoracic caused contraction in a small patch in the lower part of the muscle nearer the dorsal than the ventral edge. There was considerable overlapping in the areas affected, the contraction was chiefly in the middle strip of the muscle and the extreme dorsal and ventral edge were unaffected.

The two neuromes were surrounded by a thick mass of tissue, and it was difficult to obtain a sufficient length of the central portion of the spinal accessory for isolated stimulation. The end joined to the cerv. symp. caused a stronger contraction of the sterno-mastoid than was obtained from the cerv. symp., it caused also contraction of the trapezius. It was doubtful whether it had or had not any effect on the nictitating membrane or eye. 2.c.c. of 1 p.c. curari injected intravenously paralysed the cerv. symp. and the spinal accessory.

We have earlier[1] given an account of an experiment in which the cervical sympathetic was connected with the peripheral hypoglossal. The result was not clear, and we are repeating the experiment.

[1] Langley and Anderson. *Archivio di Fisiologia*, I. p. 507 (Exp. 2), 1904.

Lastly we have joined the cervical sympathetic with the phrenic nerve and obtained contraction of a part of the diaphragm on stimulating the 1st, 2nd and 3rd thoracic nerves in the vertebral canal (cp. above, Exp. 4).

In all these cases there was no interval appreciable to the eye between the stimulation of the nerve and the contraction of the muscle, and we think it is perfectly certain that the contraction was not produced by vascular changes.

4. THE UNION OF SOMATIC AFFERENT NERVES WITH PRE-GANGLIONIC NERVES.

There are two cases to consider here, one in which the fibres proceeding from a spinal ganglion to the central nervous system are joined to a pre-ganglionic nerve and the other in which the fibres proceeding from a spinal ganglion to the periphery are similarly connected.

An experiment of the former kind has been made by Budgett and Snodgrass[1]. They chose as afferent fibres, the fibres proceeding centrally from the ganglion of the trunk of the vagus[2]. In a cat they removed 6 millimetres of the left cervical sympathetic a little below the superior cervical ganglion. The vagus was cut just centrally of the ganglion of the trunk, and the end connected with the ganglion sewn on to the peripheral end of the sympathetic. After 85 days, the paralytic symptoms had nearly disappeared. The vagus was cut, and stimulated with moderately strong currents, 12 mm. below the ganglion it caused withdrawal of the nictitating membrane. Stimulation with strong currents, caused in addition constriction[3] of the pupil. On application of dilute nicotine to the ganglion, the nerves ceased to cause retraction of the nictitating membrane. The wound was stitched and the animal examined 22 days later. No result was obtained until induced currents slightly painful when applied to the tongue were employed, then there was retraction of the nictitating membrane. Ligature of the vagus prevented stimulation below from having an effect.

[1] Budgett and Snodgrass. *Medical Bulletin of Washington University*, Jan. 1902.

[2] The view that this ganglion is an aberrant spinal ganglion is generally accepted. And it has been shown by one of us (Langley, This *Journal*, xxiv. 1899, *Proc. Physiol. Soc.* p. xxxii.) that the ganglion sends fibres to the solitary bundle and to the grey substance latero-dorsal of the dorsal vagus nucleus.

[3] 'Constriction' is, we suppose, a slip of the pen for 'dilatation.'

The authors conclude that it is probable that the central ends of the afferent fibres of the trunk ganglion had joined the sympathetic nerve cells, but they point out that the effect obtained may have been due to an axon reflex from efferent vagus fibres growing from the central end of the vagus and sending branches to the sympathetic ganglion.

The experiment though suggestive is clearly not decisive as to the connection of afferent fibres with sympathetic cells. For besides the possibility of an axon reflex, the effect may have been due, as far as the account of the experiment shows, to sympathetic fibres running to the vagus near its ganglion, an explanation which would account for the strong current required to produce an effect.

We have repeated this experiment, with the modification of cutting the cervical sympathetic low in the neck 7 days before the final examination. Stimulation of the vagus with whatever strength of current gave no trace of sympathetic effect of any kind.

Union of vagus above ganglion of trunk to cervical sympathetic.

EXP. 8. Cat. Cervical sympathetic cut close to the sup. cerv. ganglion and about 3 cm. below the cut excised. Vagus cut 2 mm. above the ganglion of the trunk, and the end connected with the ganglion sewn to the peripheral end of the sympathetic.

138 *days later.* The paralytic symptoms were still marked. The cerv. symp. was cut low in the neck.

7 *days later.* The vagus was exposed in the lower part of the neck and up to its junction with the cerv. symp. Stimulation of it gave no effect on the nictitating membrane, eyelids, pupil, vessels of ear, or hair of face (it had no effect also on the œsophagus or rate of heart-beat). Stimulation of the sup. cerv. ganglion gave the usual sympathetic effects.

Microscopically a small filament of degenerated nerve fibres was found running from the central end of the cerv. symp. upwards attached to the vagus, and a few degenerated fibres (about half-a-dozen) were found in the cerv. symp. immediately below the sup. cerv. ganglion.

In another experiment we joined the central end of the great auricular nerve to the peripheral end of the cervical sympathetic, allowing 206 days for union. During life no sign of recovery from the paralysis was observed in the pupil, but there was apparently some in the eyelids and nictitating membrane. The central end of the sympathetic was found to have effected some though not great reunion with the peripheral end, but the end of the great auricular nerve which had been joined to the cervical sympathetic gave no trace of effect.

Union of the great auricular nerve with the cervical sympathetic.

EXP. 9. Cat. The right great auricular nerve was cut at the base of the ear. The cervical sympathetic was exposed from the side, cut about 3 cm. from the sup. cerv.

ganglion, isolated upwards for about 1·5 cm., the end drawn outwards and sewn to the central end of the great auricular nerve.

206 *days later*. On the right side, the pupil was markedly smaller, the nict. membrane farther out, and the eyelids rather closer than on the left. Both ears were cool and much the same.

The cervical sympathetic low in the neck caused moderate retraction of the nict. memb. and separation of the eyelids; also dilatation of the pupil to about ⅓ full size.

The cerv. symp. from its junction with the great auricular up to the sup. cerv. gang. gave the same effects. No reflex was obtained from it on the opposite eye; near the neurome it was doubtful whether it caused slight modification of respiration; it caused no body movement.

The peripheral end of the 3rd cervical nerve was cut near its exit from the neck muscles; the peripheral end had no effect on the eye or pupil.

The great auricular nerve centrally of its union with the cerv. symp. when uncut caused slight reflex body movement (chiefly flexion of hind limb of the same side) but either no effect on the corresponding pupil, or less than on the opposite side; after section, the end connected with the cerv. symp. gave no effect.

An experiment of a different kind was made by cutting the cervical sympathetic in the middle of the neck, and sewing the peripheral end into the subcutaneous tissue. The only nerve fibres which are likely in this case to have an opportunity of unity with the cervical sympathetic are the cutaneous afferent fibres, and efferent post-ganglionic fibres, the latter being non-medullated. 79 days were allowed for regeneration. Stimulation of the cervical sympathetic near its junction with the skin was without effect. Microscopic examination showed that 80 small medullated fibres ran into the nerve from the skin, the number decreased towards the superior cervical ganglion and near the ganglion 12 only were present. It follows we think from this, that the cutaneous fibres had not coalesced with the sympathetic fibres, but that some afferent fibres had grown down the cervical sympathetic without being able to transmit nervous impulses to the nerve cells of the superior cervical ganglion.

5. The union of pre-ganglionic with post-ganglionic nerve fibres.

The possibility of the functional union of these two kinds of fibres can be tested by excising the superior cervical ganglion. The distance between the pre-ganglionic fibres of the cervical sympathetic and the post-ganglionic fibres when the ganglion is excised, is usually less than a centimetre, so that we might naturally expect the cervical sympathetic to grow across this gap and make functional connection with the post-ganglionic fibres, especially as the former is in life constantly sending impulses to the latter.

An experiment of this kind has already been made by one of us[1] and it was found that the ocular paralytic symptoms caused by removal of the ganglion persisted, and that stimulation of the cervical sympathetic a year and eleven months after the operation had no effect.

A similar experiment has been made by Langendorff[2]. He excised the superior cervical ganglion on one side in a cat. He found that the signs of paralysis almost completely disappeared in 105 days, and that stimulation of the cervical sympathetic had its usual effects upon the pupil and eye; on microscopical examination he found no middle cervical ganglion.

We have made eight experiments on cats of various ages, excising the superior cervical ganglion of one side and leaving a varying time for regeneration. In two of these cases there was some decrease in the paralytic symptoms, and the cervical sympathetic had some effect though far from maximal. But microscopical examination showed that in both of these cases, all the nerve cells had not been removed. In one case there were some cells in the cervical sympathetic about 1½ cm. below the end of the nerve. In the other case one, though only one, of the anterior branches contained nerve cells. In both cases injection of nicotine stopped the effect of stimulating the cervical sympathetic, but did not stop the effect of stimulating the nerve strands by the internal carotid artery. In one case then there was regeneration of post-ganglionic and on the other regeneration of pre-ganglionic fibres.

In the six other cases, the paralytic symptoms on the pupil, eyelids and nictitating membrane were permanent. And in no case did stimulation of the cervical sympathetic cause any effect. The times allowed for regeneration were 183, 240, 394, 429, 438, and 476 days. One animal was a kitten 12 days old, one a half-grown cat, the other animals were full-grown cats. In one case a piece of hypoglossal nerve was inserted between the two ends of the sympathetic in order to afford a readier path for the pre-ganglionic fibres; the piece of hypoglossal nerve was absorbed and no union of the sympathetic fibres occurred. In no case were nerve cells present either in the cervical sympathetic or in the post-ganglionic nerve strands.

It seemed possible that the absence of union was due to the pre-

[1] Langley. This *Journal*, xxv. p. 417. 1900.

[2] Langendorff, *Centralblatt f. Physiologie*, 1901, p. 483; Intern. Congr. f. Phys. Sept. 1901. Langendorff mentions two cases. In the second the anterior branches were tied, but the ganglion was not removed. Here reunion of the post-ganglionic fibres would naturally occur.

ganglionic fibres having a definite length, and to their being unable to grow out sufficiently to reach the post-ganglionic fibres, notwithstanding that the distance was only about a centimetre. This possibility was however negatived by experiment, for we found that the distal end of the cervical sympathetic of one side was able to make functional union with the proximal end of the cervical sympathetic of the opposite side[1].

Junction of cervical sympathetic of one side with the cervical spmpathetic of the opposite side.

Exp. 10. Cat. Rt. cerv. symp. cut a few millimetres before it entered the sup. cerv. gang.; left cerv. symp. cut low in the neck. The right nerve was then turned backwards, taken over the trachea and joined to the peripheral end of the left nerve.

169 *days later.* The central end of the left cerv. symp. gave no effect. The central end of the *right* cerv. symp. gave on the *left* side all the effects normally produced by sympathetic stimulation; there was maximal dilàtation of the pupil, strong retraction of the nictitating membrane, and separation of the eyelids, projection of the eye, complete pallor of the vessels of the ear and of the nasal mucous membrane and erection of hair in the face area. The effects ceased on applying 1 p.c. nicotine to the left sup. cerv. gang.

The distance from the neurome to the left sup. cerv. gang. was 62 mm. *i.e.* the right sympathetic nerve had lengthened by about 62 mm.

The absence of union of the pre-ganglionic with the post-ganglionic fibres was not due to the one consisting of medullated and to the other consisting of non-medullated fibres, since the anterior rami of the superior cervical ganglion contain normally numerous medullated fibres, and in each of our cases regeneration of post-ganglionic medullated fibres had occurred[2].

We conclude then that pre-ganglionic fibres though conducting in the same direction, and having the same function, as post-ganglionic fibres are incapable of making functional union with them.

6. Union of post-ganglionic fibres with pre-ganglionic fibres.

We have seen that the pre-ganglionic fibres of the cervical sympathetic readily unite with the similar fibres of the opposite side. The following experiment gives evidence that the post-ganglionic fibres cannot unite with pre-ganglionic fibres, nor make connection with the nerve cells of the opposite superior cervical ganglion. Further experiments are however desirable.

[1] A similar elongation of the cervical sympathetic occurred in Exp. 1 which we have given in *Archivio di Fisiologia*, I. p. 506, 1904. In Exp. 11, given later on in this Paper, there was also considerable elongation of the cervical sympathetic.

[2] The cause of the re-formation of the post-ganglionic medullated fibres we shall deal with in a later Paper.

Union of the post-ganglionic fibres of the cervical sympathetic of one side with the pre-ganglionic fibres of the opposite sympathetic.

Exp. 11. Cat. The left cerv. symp. was cut a little below the middle of the neck, the end passed under the trachea and sewn to the anterior branches of the right sup. cerv. gang. close to the ganglion.

143 *days later*. The right cerv. symp. caused normal effects on the right side, *i.e.* a good many of the post-ganglionic fibres had diverged from the path afforded them by the nerve to which they were sewn and had joined their own peripheral ends. It caused on the left side a slight effect on the nictitating membrane and eyelids; a very slight effect on the pupil (the trifling dilatation produced was prompt, all round the pupil, but more on the malar than on the nasal side); erection of one or two hairs in the face area; and slight to moderate pallor of the ear.

After application of warm 1 p.c. nicotine to the right ganglion, the right cerv. symp. had (for a time) no effect on the right side, its effect on the left side was unaltered, *i.e.* the pre-ganglionic fibres producing the effect on the left side did not end in the cells of the right ganglion but ran through it.

After application of warm 1 p.c. nicotine to the left sup. cerv. ganglion, the right cerv. symp. had no effect on the left side (the paralysis however was of less duration than usual with sympathetic ganglia), *i.e.* the pre-ganglionic fibres which ran through the right ganglion ended in the nerve cells of the left ganglion.

Microscopic examination showed that about ⅓ of the fibres of the anterior branches of the rt. sup. cerv. gang. were firmly joined to the opposite cerv. symp.; medullated fibres were present in the whole intervening region. There was also a number of nerve cells, showing that in one of the anterior branches the nerve cells had stretched farther forward than usual, and these had been cut through, thus cutting through a small number of pre-ganglionic fibres. The experimental results indicate that these pre-ganglionic fibres were the only ones to make connection with the cells of the opposite sup. cerv. gang.

7. The union of post-ganglionic nerves with somatic efferent nerves.

We have, so far, only made one experiment of this kind, viz. the union of the anterior branches of the superior cervical ganglion with the hypoglossal nerve (Exp. 12). In this experiment, the cervical sympathetic did not acquire any action on the muscles of the tongue, *i.e.* the post-ganglionic fibres did not unite with the hypoglossal fibres supplying the tongue muscles. That there was an opportunity of union, is indicated by the fact that the cervical sympathetic caused marked pallor of the corresponding half of the tongue after isolation of the sympathetic-hypoglossal strand, *i.e.* the post-ganglionic fibres of the sympathetic had united with the post-ganglionic vaso-motor fibres of the hypoglossal. On the other hand the experiment was not quite satisfactory since the central ends of the cut nerves had partly rejoined their peripheral ends, and this would to some extent interfere with the union in question.

Union of post-ganglionic fibres of the superior cervical ganglion with the peripheral end of the hypoglossal.

Exp. 12. Cat, half-grown. The hypoglossal nerve was cut near the skull, the anterior branches of the sup. cerv. gang. were cut just beyond the ganglion, and sewn to the peripheral end of the hypoglossal.

261 *days later*. The rt. cerv. symp. caused considerable though not complete pallor of the right half of the tongue; the effect was rather greater than that produced on the left half of the tongue by the left cerv. symp. It had no effect upon the tongue muscle. It had however some effect on the pupil and eye, so that part of the anterior branches had remade their original connections.

The rt. hypoglossal nerve from the neurome onwards caused contraction of the muscles of the tongue with some pallor, on cessation of the stimulus there was flushing (as normal) and fibrillar twitchings, especially at the edge. Thus the central end had remade connection with the peripheral end.

After isolation of the sympathetic and the connected hypoglossal, the sympathetic caused pallor of the tongue, but no other effect.

Microscopically a small non-medullated strand was traced from the superior cerv. ganglion to the hypoglossal, but the main strand curved away from the nerve. Both the hypoglossal and the internal carotid nerve-bundles contained many medullated fibres, and a considerable number of the fibres in the proximal end of the internal carotid bundles were larger than normal, about the size of the hypoglossal fibres.

Summary of results.

1. When the central ends of two limb nerves are joined, no functional union takes place between them; impulses set up in one nerve cannot pass across the neurome to the other nerve. The fibres of one nerve may grow a short distance down the other nerve but the distance is at most short. This confirms the result obtained by Schiff and by Stefani. The result has also been recently confirmed by Bethe.

2. According to Bethe when the peripheral ends of two limb nerves are joined in puppies functional union of the two nerves may take place. In our experiments on rabbits and cats, such functional union did not occur.

3. When the central end of a limb nerve has an opportunity of joining with two peripheral nerves, stimulation of one peripheral nerve, after complete severance of the conjoined nerves from the central nervous system, may cause contraction of the muscles innervated by the other. We consider this to be an axon reflex, set up in fibres from the central end, one branch of which has joined one peripheral nerve and the other branch joined the other peripheral nerve.

4. When one of the peripheral nerves consists entirely of afferent fibres an axon reflex may still be produced by stimulating it. Since efferent fibres do not so far as is known unite with afferent fibres, the

axon reflex obtained supports the view that regeneration takes place by a down growth of axis cylinders.

5. The crural nerve can make functional union with the sciatic and so be artificially lengthened. This is in harmony with Bethe's observation that the sciatic can be elongated by joining it with the sciatic of the opposite side. The cervical sympathetic can also be elongated by joining it to the cervical sympathetic of the opposite side.

6. We do not find that the internal saphenous nerve when joined to the sciatic acquires a motor effect.

7. The phrenic nerve when united with the cervical sympathetic can cause the usual effects produced by stimulating the latter nerve.

8. We confirm Mislavski's result that the cervical sympathetic can unite with the recurrent laryngeal nerve and cause movement of the vocal cords. The movement is due to contraction of the thyro-arytenoid muscle and to unilateral contraction of the arytenoideus muscle. We find also that after functional union has taken place, section of the cervical sympathetic causes degeneration of the medullated fibres in the recurrent laryngeal, except for a few which arise from the superior laryngeal nerve.

9. The cervical sympathetic can unite with the phrenic nerve and cause contraction of the diaphragm.

10. The cervical sympathetic can unite with the spinal accessory nerve and cause contraction of the sterno-mastoid muscle.

11. We do not find that either (*a*) the afferent fibres proceeding centrally from the ganglion of the trunk of the vagus or (*b*) the afferent fibres proceeding peripherally in the great auricular nerve or (*c*) cutaneous afferent fibres, can unite with the peripheral end of the cervical sympathetic in such a way as to transmit nervous impulses to it or to the superior cervical ganglion.

12. We do not find that the cervical sympathetic—after excision of the superior cervical ganglion—can make functional connection with the fibres leaving the anterior end of the superior cervical ganglion. We consider then that pre-ganglionic fibres cannot make functional connection with post-ganglionic fibres.

13. We do not find that the post-ganglionic fibres leaving the anterior end of the superior cervical ganglion can form functional connection with the pre-ganglionic fibres of the opposite cervical sympathetic (one experiment only).

14. We do not find that the post-ganglionic fibres leaving the anterior end of the superior cervical ganglion can make functional

connection with the hypoglossal fibres supplying the tongue muscles, although they do this with the vaso-motor fibres of the hypoglossal (one experiment only).

Remarks and General Conclusions.

The nerve fibres with which we deal are obviously divisible into four classes, (*a*) the efferent fibres which run from the central nervous system and end in multi-nuclear striated muscle cells (efferent somatic fibres), (*b*) the efferent fibres which run from the central nervous system and end in ganglion cells (pre-ganglionic fibres), (*c*) the efferent fibres given off by the peripheral ganglia (post-ganglionic fibres), and (*d*) afferent fibres connected with nerve cells in the posterior root ganglia.

From a consideration of the whole of the observations which have been made upon the cross union of fibres we draw the following conclusions, though we readily admit that the evidence is still incomplete.

1. The central end of an efferent fibre can make functional connection with the peripheral end of any other efferent fibre[1] of the same class whatever be the normal actions produced by the two nerve fibres.

For the fibres of Class *a* this is generally recognised as regards the nerve fibres which run to the muscles of the body and face, and we think there is sufficient ground for including with these the nerve fibres which supply the striated muscle of the tongue, pharynx and larynx.

Evidence with regard to the nerve fibres of Classes *b* and *c* has been given by one of us[2] elsewhere.

2. The central end of any efferent fibre of Class *a* can make functional union with the peripheral end of any fibre of Class *b*, and the central end of any fibre of Class *b* can make functional connection with the peripheral end of any fibre in Class *a*.

There is then a fundamental resemblance between the nerve fibres of these two classes, *i.e.* between all the efferent fibres which leave the spinal cord whether they end in multi-nuclear striated muscle or in peripheral nerve cells.

[1] It is known that the afferent fibres of one nerve can unite with the afferent fibres of another nerve, but the evidence is insufficient to show whether the nerve fibres giving rise to one sensation can unite with fibres giving rise to another sensation.

[2] Langley. This *Journal*, xxii. p. 215. 1897.

It is to be noted that when a somatic efferent fibre 'unites' with a pre-ganglionic fibre its termination is shifted from striated muscle to nerve cells, as can be shown by applying nicotine to the nerve cells.

3. The experiments we have given above indicate that the peripheral ends of cut nerve fibres exert a chemiotactic influence on the central ends, that this chemiotactic influence is greater between the efferent fibres of Class *a* amongst themselves, and between the fibres of Class *b* amongst themselves, than it is between the efferent fibres of one class and those of the other, and it seems to us probable that this chemiotactic influence has numerous gradations.

There are several earlier observations bearing on this point.

Bidder in his experiments on cross union of the hypoglossal and lingual was struck with the way in which the nerve fibres left the nerve to which they were sewn and rejoined their own peripheral ends. Similar facts have been observed by all subsequent observers.

Schiff dwelling on the fact of the ready union of one motor fibre with another, and of the difficulty or impossibility of uniting sensory and motor fibres came to the conclusion that the nutritive conditions of the two kinds of nerves must be essentially different in nature.

In the experiments on the union of pre-ganglionic and post-ganglionic nerves made by one of us it was found that the great majority of the nerve fibres in regeneration made their normal, and that a few made abnormal, connections; it was suggested that this must be due to some chemiotactic influence.

Forsmann whose observations are strongly in favour of an attractive influence being exerted by nerve substance on central outgrowing nerve fibres, does not find that regeneration is quicker with union than with cross union of the nerves to the limbs; but it seems to us that the question of chemiotactic influence for such nerve fibres would be better determined by stimulating the nerve roots after regeneration of the sciatic and observing what normal and what abnormal connections have been made.

4. From what has been said in Clause 2 it follows that we may reduce the four classes of nerve fibres to three as regards the possibility of their union.

A. Efferent fibres proceeding from the spinal cord.
B. Post-ganglionic nerve fibres.
C. Afferent nerve fibres.

We conclude from the experiments given above that functional union is not possible between fibres of Class A and Class B. With regard to the union of afferent with efferent fibres and *vice versâ*, the term functional union is inappropriate. The experiments of Schwann and Schiff show that in the nerves of the limbs afferent fibres when joined to efferent fibres do not acquire any motor action, we have given an experiment confirmatory of their result; the observations of Vulpian and others show that the proper afferent fibres of the lingual nerve do not acquire motor power when joined to the hypoglossal nerves; and our own experiments go far to show that afferent fibres do not acquire a motor effect when they are joined to pre-ganglionic fibres. We conclude then that afferent fibres are incapable of uniting with efferent fibres in such a way as to give motor effects, from which it follows that afferent nerve fibres cannot coalesce with efferent fibres.

The observations do not exclude the possibility that afferent fibres may grow down the course of the efferent fibres, and form afferent nerve-endings, which from character or position, are incapable of transmitting nervous impulses to muscle, gland, or motor nerve cells. Hence if the ordinary regeneration of a cut nerve consists in a growth from the central ends, there might be a similar regeneration when sensory nerve is joined to motor nerve, though the regeneration in this case would have no appreciable functional value.

The experiments which have been made on the union of fibres of Classes A and B with fibres of Class C show we think fairly conclusively that a motor nerve when united with a sensory nerve does not acquire motor power. But this might be due on the theory that the fibres unite, to the afferent nerve-endings being unable to transmit impulses to the muscles, and on the theory of central out-growth to the new motor endings formed being out of range of the muscles.

Still as we think sensory fibres do not coalesce with motor fibres, we think it unlikely that motor fibres should coalesce with sensory, and we conclude provisionally that the nerve fibres of the three classes mentioned above are incapable of coalescing with one another. In all cases the fibres of the central end grow some distance into the peripheral end, and the extent of out-growth is probably dependent on the nutritional value of the peripheral nerve.

5. In Exps. 7 and 8 afferent fibres grew out amongst the nerve cells of the superior cervical ganglion; the fact that the fibres did not transmit impulses to the ganglion was we think due either to the fibres only forming nerve-endings in appropriate surroundings, or to the nerve-endings being unable to affect the nerve cells. And similar considerations apply to other cases of cross union.

6. Whether the regeneration which takes place when fibres of the same class are united is due to coalescence or to down growth we regard as an open question notwithstanding the interesting researches of Bethe. We hope however that a microscopical examination of the kind of nerve endings formed in the cross union of somatic and pre-ganglionic fibres may help to decide the question. On the one theory the nerve-endings should have the character of the endings of somatic nerve fibres, and on the other that of the endings of pre-ganglionic fibres.