I hereby declare that this Thesis has been composed by myself, and that the photographs are also my own work.

Robt Kennedy.

The four operations were performed by me in the Western Infirmary, Glasgow (Wards XII and XIV) in the capacity of assistant to Dr. Patterson.

About 120 series of sections were examined, and a selection of these, including those from which the microphotographs were taken, lies in the Zoological Laboratory of the University, where most of the sections were prepared, and where, if desired, they may be inspected.

Studies
on the
Regeneration of Nerves,

A Thesis for the Degree of M.D.,

Presented to the Senatus of Glasgow University,

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Part I.

Although so many investigations have been published on the subject of regeneration of nerves, there is still much diversity of opinion on the process by which injured nerves are repaired. Almost till the beginning of the present century, the view expressed by Galen[x], that nerves once divided are incapable of being again restored, seems to have been generally accepted. It is true that Guy de Chauliac[xx] not only speaks of the perfect restoration of divided nerves, but even recommends the operation of suture; but as he speaks at once of nerves and tendons, some doubt must remain whether we can accept his remarks as really referring to nerves. Be this as it may, it is certain that towards the end of last century, the general belief was that nerves are incapable of reunion after division.

The first experimental research which showed the possibility of reunion, was made by Cruikshank (2.) in 1776. His experiments were made on dogs, and consisted in dividing the vagus and sympathetic in the neck, with the object not of investigating nerve regeneration, but of studying the dependence or otherwise of the internal organs on these nerves. In his first experiment, he divided the nerves of one side, and ten days later those of the

[x] After Létiévant (82.) l.c., p. VIII. The numbers in brackets refer to the Bibliographical Index, page 138.

[xx] Guido de Cauliaco. Chirurgia, Lugd., 1537, p. 114. "Ego vidi et audivi in multis nervos et thenanton incisos; et eos ita restauratos cum sutura et aliis auxiliis, quod erat postea incredibile ipsos fuisse incisos."

other. The animal died seven days later, and on examination, the nerves first divided were found united "by a substance having the same colour as the nerve, but not having the fibrous appearance". This he states was regeneration of the nerves, "a circumstance never hitherto observed". He thought that given a longer time for the nerve first cut to regenerate, the animal might survive the division of the nerve of the opposite side, and to prove this, he divided the vagus of the right side, in another dog, and three weeks later removed a portion from the vagus of the left side. The animal got perfectly well. Eighteen days later, he killed it, and found the nerves both united, the cut ends of the right nerve being united by a mass of greater thickness than the nerve, while those of the left were united by a narrower portion. The results of this investigation were communicated to the Royal Society by Hunter on 13th June, 1776; but the prevailing opinion being that the nerves were united simply by connective tissue, the paper was not thought worthy of publication until nineteen years later, when its importance was recognised. The preparation, however, was placed in William Hunter's museum, and was the means of stimulating others to further researches. I found this preparation (Plate I) recently, in the Hunterian Museum in Glasgow, its history unknown, and was easily able to identify it from the drawing published with the paper.[x]

Fontana (3.) who saw the preparation in Hunter's museum in 1778, commenced a research on rabbits, particularly with the object of determining whether the mass, which reunites the ends of a cut nerve, is composed of nerve substance, or is simply cicatricial connective tissue; for he states that it was this latter view, which Hunter took of Cruikshank's preparation. Fontana saw in two of his vagus sections reunion occur, and saw the passage of the nerve fibres, which he had discovered in normal nerve, through the intermediary mass, and concludes that nerve regeneration is possible.

Monro (4.) soon afterwards found in a frog reunion of the sciatic nerve, which had been divided a year previously; but concludes against reunion by nerve substance, as in his experiment he could not find

x My thanks are due to Professor Young for his kindness in permitting me to photograph this preparation. The delay in printing Cruikshank's communication until after the death of William Hunter, accounts for the history of the preparation having been so long unknown.

return of sensation or motion, although the limb did not undergo the slightest trace of atrophy.

Michaelis,[x] who had also seen Cruikshank's preparation, made experiments on dogs, and found as a rule regeneration of the portion excised. He made an experiment the priority of which is usually given to Haighton, to show that the function is not restored by means of anastomosis or supplementary supply, theories which were afterwards brought forward to explain return of function after nerve section. His experiment was performed on a dog, and consisted in excising one inch from the phrenic nerve (? vagus). The animal recovered from this in a few days. One and a half months later he divided the nerve of the left side, and on the third day recut the first nerve, which by this time had reunited. The animal immediately showed the symptoms of division of both nerves, and died soon afterwards.

Arnemann (5.) who published the results of his experiments soon afterwards, came to the opposite conclusion. He never found regeneration. He admits the reunion of the ends of a divided nerve, but this is merely

[x] After Arnemann (5.)

connective tissue, the result of the growth of the nerve sheath, and surrounding connective tissue. He admits, however, the possibility of a reunion which allows re-establishment of function; but this is the result of the close approximation of the ends, and the absence of inflammation, the nerve current being then able to overstep the slight obstacle. He conducted two experiments on dogs to determine if nerve suture could bring about this favourable result; but his results were so disastrous that he thinks nerve suture an unjustifyable operation.

Similar results unfavourable to the possibility of regeneration of nerves, had been obtained by several other workers after Arnemann, when Haighton (6.) commenced his experiments. He worked upon the same lines as Cruikshank had, and states that the differences of opinion which then existed, depended on the fact that there was difference of opinion as to what the normal structure of nerves was, and that until this was known, the only way to settle the matter was to take the physiological proof. He, therefore, repeated Cruikshank's experiments. He first divided both vagi and sympathetic nerves in a dog, and found death on the following day. Next he divided the vagus and sympathetic of one side, also in a dog, and six weeks later divided the nerves of the opposite side. By a month the dog had recovered, and by six months was as well as before the operation. He explained this as due to the reproduction of the cut vagus in the six weeks; and the gradual improvement in the dog's condition, he explained as the result of the gradual restoration of the nerve which had been cut at the second operation, and the gradual further improvement of the nerve first cut. The dog was kept for nineteen months, and was used as a "yard dog". At the end of that time, wishing to prove that the result was really due to nerve regeneration, he divided the nerves of both sides again, above the points of previous section, and the animal died on the following day. This experiment was much the same as that conducted by Michaelis, who, however, allowed his dog to live three days only after the division of the second nerve.

Haighton did not attempt to prove

the regeneration of nerves anatomically, and it was scarcely possible that this could have been done satisfactorily by the microscope at that time; but, two years later, J. C. H. Meyer (17.) published the results of his investigations, which had been conducted by a new method. Reil had shown that nerve tissue resists the action of nitric acid, while the connective tissue is destroyed, and Meyer took this test to settle the point whether functional return is accompanied also by anatomical regeneration. Arnemann's statement that the nerve current can spring across a slight barrier, had of course not been answered by the experiments of Haighton. Meyer, then, found in the peripheral nerves of the dog, that in little over a month function returned after section. When the restored nerves had been subjected to the action of nitric acid, nerve substance was left not only in the bulbs formed at the cut surfaces, but there was a string of nerve substance passing across between the two ends. Another experiment made by him is of importance, as tending to show the regeneration of nerves cut off from their centres in the spinal cord. He cut the tibial, and thirteen days later the sciatic, and when examined at the end of sixty-eight days, the tibial was found united by a strand of nerve substance; and the sciatic was not united.

The balance of opinion was still against the possibility of nerve regeneration, and it was thought that Haighton might have mistaken the nerves, which he cut, for the vagi.× Prévost (10.), therefore, repeated Haighton's experiments on five kittens, in each of which he first resected two and a half lines from the left vagus. The right vagus he cut in one at the end of a month, death resulting in fifteen hours; in another at the end of two months, ending fatally in thirty six hours; and in two at the end of four months, and in fourteen days both cats were well. To prove that this recovery was not due to anastomoses, he then cut the right vagus above the point at which it had previously been cut; and the animal remained well. The left vagus he then recut at the end of thirty six hours, death resulting in thirty hours. He then submitted the united nerve to microscopical examination, and states that he saw the passage of nerve fibres through the intermediate mass from one end to the other.

The doubt which some still held, of

× vide Magendie (8.)

the possibility of nerve regeneration, seems to have been finally dispelled by the work of Steinrück (14), published in 1838. He conducted fifty experiments on frogs and rabbits, chiefly on the sciatic nerve, but in some cases on the vagus, infraorbital, and hypoglossal, in which he either simply divided or resected a portion. He allowed many of the animals to live a long time, until sensation and motion were perfectly restored. He concludes that under favourable conditions, reunion of the divided nerve occurs, first by a connective tissue bond, in which ultimately are developed nerve fibres, which differ from the old neither in physical nor in chemical properties. The health of the animal must be fairly good, and the surrounding conditions favourable, and the time taken for the restoration of function varies from five weeks to one or two years, and he notes that sensation usually returns before motion. He found that the new fibres formed in the uniting mass are produced both from the central, and from the distal segments of the nerve.

The discovery by Remak* in 1837 of the "primitiv Band", confirmed two years later by Purkinje*,

*After Ranvier (102) Tom. I, p. 29.

and called by him the axis-cylinder, and the discovery by Schwann[x] in 1839 of the "membranous sheath", now called the sheath of Schwann, first placed the study of the histological changes in a nerve after section on a stable foundation. Hitherto the observations made had been directed only to the determination of the possibility of a divided nerve being functionally restored by reunion by means of nerve substance, and from the time of Steinrück with few exceptions,[xx] the possibility is confirmed by all observers. But with Nasse (15.) a new subject of study was begun, namely, the changes which ensue in the nerve after division, and before restoration has commenced. This author studied the changes which ensued at the point of section in the sciatic in frogs and rabbits, and found that after section destruction of the primitive fibres took place, the fibre breaking up into irregular cylindrical portions, ending in fatty degeneration with absorption, ultimately the whole fibre including the sheath of Schwann disappearing. He also found that the new fibres are smaller than the old and of different appearance, and that the cicatricial substance between the divided ends can change into nerve substance.

x After Ranvier (102), Tom. I, p. 29.   xx vide Hutin (33.)

Günther and Schön (16.) in the following year corroborated Nasse's discovery, and consider this change in the structure of the nerve as the cause of the speedy loss of conductivity in the distal segment of a divided nerve, and view the degenerative changes as the result of lowered vitality by the separation of the nerve from the centre. They found also that the distal segment of a divided nerve, which has lost its irritability and normal structure, can, if not too long separated, reunite with the central end, and regain its structure and functions, and they regard this reunion as effected from both the central and the distal segment.

These observations on the degeneration of the distal segment were corroborated by Stannius (18.), who was the first to make the observation that the degenerative changes are not confined alone to the immediate neighbourhood of the wound, nor even to the main distal stem, but that even the finest ramifications of the nerve in the muscular fibres show signs of the degenerative process. But this was only an isolated observation, and he gives it only as such, without regarding it as proved to be a general law. His observations were made on toads and frogs, and he found that the loss of irritability of the distal segment took about eight and a half days to become complete, and that the loss took place centrifugally.

These earlier observations on degeneration of nerves were taken up by Waller (20, 22 to 29) in 1849. He proved that the degeneration observed by Nasse, is not confined to any limited section of the distal segment of a divided nerve, but that it extends to the ultimate ramifications. His observations were made principally on frogs, in which he had divided the glossopharyngeal nerve of one side. The animals were allowed to live from one to four months, and, at increasing intervals from the time of section, he examined the state of the terminal ramifications in the fungiform papillæ of the tongue. By snipping off the papillæ by means of sharp scissors, he was able to examine the microscopical appearance of the nerve endings in the living state. He also examined the degenerative processes in his own tongue, by applying a ligature round the base of the papilla, and snipping off the papilla at the end of the third day. By these observations, and by examining also the distal stem of the glossopharyngeal in the frog, and the distal segment of the divided sciatic in rabbits, Waller showed that degeneration after section of a nerve extends from the point of section onwards to the ultimate ramifications. He also found that the central segment of the nerve remained unaltered. Pursuing his investigations further, he showed that on dividing both roots of a spinal nerve above the ganglion on the posterior root, none of the sensory fibres below the point of section degenerate, while the motor do; and of the portions of the roots above the point of section, the posterior degenerates, while the anterior remains normal. On dividing the posterior root below the ganglion, and leaving the anterior root intact, he found that the sensory fibres below the point of section degenerate, while the motor remain intact. Thus Waller was led to establish the law of dependence of the nerves on trophic centres, which, he showed, lie for the motor fibres in the spinal cord, and for the sensory in the ganglion on the posterior root; and to show that the degeneration resulting in the nerve fibre after section depends upon its separation from its trophic centre. He gives this also as a new method for the study of the nervous system, and was able to trace by its means the ramifications of the ultimate nerve fibres in the frog's tongue. He cut one glossopharyngeal, and showed by the ultimate degeneration, that some of its fibres cross the middle line into the region supplied by the nerve of the opposite side, and also showed the existence of anastomoses with the hypoglossal nerve.

He divides the degenerative changes into three periods, the first being found in frogs in summer at the end of four or five days, at which period the intratubular contents of the papillary fibres are interrupted by transverse lines, and notes that this stage can only be accepted as a degenerative change by examining living fibres and comparing with the normal papillary nerves of the opposite side of the tongue, as similar changes are produced in perfectly normal nerves post mortem, or by treatment with reagents. His second period is developed by ten days, and then the tubes are filled with round or oblong masses, as if the contents had divided into two constituents. In his third period the tubes are filled with black granules, which resist the action of acids and alkalies. These are ultimately absorbed, leaving the nerve composed simply of collapsed membranous sheaths, resembling strands of connective tissue, having here and there still remains of the black granules.

The axis-cylinder is not expressly mentioned by Waller, but as he refers to the whole intra-tubular contents, he evidently means that this structure disappears along with the myeline sheath. Budge (21.), who had worked partly in conjunction with Waller, came to the same conclusions.

According to Waller, the old fibres never recover their functional activity or structural characters, and reproduction of the nerve after section occurs not only in the intermediate portion uniting the cut surfaces, but also throughout the distal segment to the ultimate ramifications. In frogs in which the glossopharyngeal had been divided three to four months previously, he found that, while the papillary nerves contained tubes in the third period of degeneration, there were also newly formed fibres lying between the old. These new fibres he found much narrower (1/4 - 1/8) than the original fibres, pale, with no double contour, of unequal diameter, with fusiform nuclei at intervals, and closely re-sembling the fibres in the young frog, just after the tadpole stage. He holds these fibres to be new formations, as they always lay among the old fibres, never within them. He found that these new fibres were developed centrifugally, as they became more numerous as higher levels of the nerve were examined; and they are also dependent upon reunion, as they were never seen, until the intermediary portion contained new fibres. At the end of nine months, almost all the papillæ contained new fibres.

Waller's view, then, is that the result of section of a nerve is inevitable destruction of the nerve fibres throughout the distal portion; and that regeneration only occurs, when the distal segment becomes connected to the central; and that the formation of new fibres begins after the old are degenerated, starts in the intermediate portion, and travels on to the ultimate ramifications, these being found in the frog to contain regenerated fibres at the end of nine months.

This view of regeneration was widely accepted, and the first publication to throw doubt upon it was that of Paget (30.) in 1853. In this publication, he gives an account of two cases of restoration of function after division of the nerve, effected so speedily that there was scarcely time for the process described by Waller to have occurred. The first case was that of a boy, in whom the median and radial nerves had been divided a little above the wrist. The nerves were not sutured, and yet function, which had been totally lost directly after the injury, began to return in the median distribution in ten days, and was nearly perfect in a month. The second case was that of a boy, whose hand had been almost severed from the forearm at the wrist, the median and radial nerves being divided. Sensation began to return in from ten to twelve days, although no sutures were employed. These cases Paget gives as examples of healing "by immediate union, or by primary adhesion with an exceedingly small amount of new substance". He accepts the process described by Waller for cases in which such early union fails.

These clinical observations were supported by Schiff (31.), who made his observations on cats and dogs. He admits fatty degeneration of the whole distal segment of the nerve, but differs from Waller in that he maintains that the sheath of Schwann and the axis-cylinder remain unaltered. In the axis-cylinder, even after four months without reunion, he could find no change microscopically or to reagents, although the portion of nerve was no longer irritable. He thinks that Waller's new fibres were simply the old, deprived of the myeline sheath, indeed old fibres at the ultimate stage of their degeneration; and that the fusiform nuclei were simply the nuclei of the old fibres, made visible by the removal of the myeline. Schiff, like Paget, saw recovery of function after seven to thirteen days, and believes that the new fibres are the old restored by re-accumulation of the myeline. In experimental division of the lingual and infra-orbital nerves, where he examined the distal portions in from three to four weeks, he found many of the fasciculi, which contained only restored fibres without any trace of degenerated fibres; and, in other cases, tracing the restored fibres, he saw that at intervals traces of the degenerated myeline remained.

Bruch (32.) supports the Wallerian doctrine of degeneration, but holds that the change is a kind of coagulation similar to that which occurs after death. He never saw simple fatty degeneration, and

and in this he is supported by most of the later writers. But like Schiff, he holds that the change in the fibre can be compensated for, with return of function and structure in the old fibres, if reunion occurs. A cat in which he had divided the sciatic, had recovered function perfectly, and on examining the seat of section four months after the operation, he found to the naked eye no trace of cicatrix, and it was only on stretching the nerve that the seat of section was seen. Microscopically he found here that the fibres above and below were normal, and that at the seat of union there was on each a slight constriction on the sheath of Schwann. The axis-cylinders were continued across, and the only difference was that the myeline sheath at this spot was more transparent. He inclines to the view that primary union can occur.

An important paper was published in the following year by Lent (34), in which he admits the fatty degenerative change, but holds that the empty sheaths of Schwann are left with their nuclei, which were previously hidden by the myeline. He notes with Schiff, that there are two kinds of degeneration one the immediate result of trauma, affecting both the central and distal ends, and the other paralytic, due to the separation from the centres, affecting the whole distal segment, and leaving this ultimately composed simply of the collapsed sheaths of Schwann with their nuclei. The paralytic degeneration begins in the whole distal segment down to the last ramifications simultaneously, but proceeds more rapidly in the finer twigs. He thinks with Schiff, that Waller's new fibres were simply the old empty sheaths, and traced the degenerative steps up to this point; and holds that it was accidental that Waller did not see them, till new fibres were formed in the intermediary portion. He maintains that the old fibres become gradually restored after reunion is effected. He found that in the process of reunion, at both the central and distal ends, the nuclei of the old fibres proliferate; and the sheath with its nuclei extends into the intermediary mass, and when reunion is complete the mass contains myeline fibres; but he does not know how the formation of the myeline and axis-cylinder here occurs. He does not agree with Schiff that the axis-cylinder is retained in the distal segment, and holds that in regeneration it is formed anew. He does not agree with Bruch that reunion by first intention can occur. He finds that the regenerated nerve has the appearance of an embryonic nerve at first, the fibres being the old, deprived of their axis-cylinder and myeline sheath, and that as reunion occurs the axis-cylinder and myeline sheath are gradually reformed, the most important structure for this reformation being the sheath of Schwann with its nuclei.

Schiff (35.) wrote in answer to Lent maintaining the persistence of the axis-cylinder, which he states can always be brought out by treatment with solution of corrosive sublimate. He does not agree that there is proliferation of the nuclei of the old sheath at the seat of section, and thinks that the perfect restoration by first intention described by Bruch and denied by Lent, occurs often.

From the time of Waller's investigations, the view that the distal segment of a divided nerve, in addition to undergoing degeneration throughout its extent as a result of separation from its centres, is incapable of being regenerated, until united again to its centres, had been received without contradiction. While confirming the ultimate degeneration as a result of separation, the researches of Philipeaux and Vulpian (38, 39, 45), published during the year 1859, showed that the regenerative capacity of the distal segment of the nerve is not dependent on a restoration of communication with the centres. As early as 1828, Flourens (9.) had published the result of an experiment made to determine, whether after section of two neighbouring nerves and cross suture, the proximal segment of the one nerve could unite with the distal segment of the other nerve. In a fowl in which he had in this way cross sutured the proximal segment of the nerve supplying the under muscles of the wing, to the distal of that supplying the upper muscles, and vice versa, cross union had been effected, and irritation of the proximal segment of the lower nerve induced contractions in the muscles supplied by the upper nerve, and vice versa, thus showing that at least the motor portions of mixed nerves are capable of cross union. Bidder (17.) in 1842, had investigated in dogs the possibility of union of functionally different nerves, by suturing the proximal end of a divided hypoglossal to the distal end of the divided lingual, and vice versa, but with negative results. Gluge and Thiernesse (37.) in 1859 had repeated Bidders experiments, and had concluded that the sensory nerve is incapable of becoming united to the motor functionally; but found in the course of their investigations that after four months of separation from the centres, the distal segment of the nerve was still capable of inducing on irritation strong contractions in the muscles This Gluge and Thiernesse regarded as irritability of the distal segment retained, not regenerated. Philipeaux and Vulpian in repeating these experiments on cross suturing, and finding reunion and regeneration in the distal segment of the hypoglossal after suture to the proximal segment of the vagus, wished to find whether the distal segment of the hypoglossal would not have regenerated, independently of its connection to the vagus. In one of their experiments (39. Exp. II), they resected a portion from the hypoglossal in a dog, and on examination in eighty-four days, no reunion of any kind had occurred; and yet the distal segment contained young regenerated fibres. In other cases (39. Exp. III), examined forty-six and forty-seven days after the resection, young fibres were found present, in addition to the remains of the degenerated fibres; and yet reunion had failed. In another experiment (39. Expt) the progress of events was well shown. A portion of the hypoglossal having been excised in a dog, the examination was made **two** months and seven days after the operation, and showed that signs of degeneration were still present, and that regeneration was in its earliest stage. On electrical stimulation, no contractions could be induced in the muscles. This animal was allowed to live, and was examined again in four months and twenty days from the time of the original operation. There was still no reunion of the divided ends of the nerve, but now irritation of the distal segment induced strong contractions in the muscles, and microscopical examination showed plentifully new nerve fibres. Similar results were obtained with the distal segment of the divided lingual in the dog, and also with the sciatic and median in the guineapig. Thus Philipeaux and Vulpian explained the observation of Gluge and Thiernesse, that the distal segment of the nerve was irritable at four months from the date of separation; for this was not retained irritability, but the nerve had in the interval become regenerated. They found that in from six weeks to six months the distal segment of a divided nerve had undergone complete degeneration, with the exception of a few fibres which retained their normal aspect. These fibres were derived from neighbouring nerves by anastomosis. Thus, in the lingual, there were a few normal among the degenerated fibres, these being derived from the hypoglossal; and in the distal segment of the hypoglossal, pain was produced by pinching with forceps, this being the recurrent sensibility discovered by Magendie, and explained later by Claude Bernard (36.) as due to anastomotic fibres. The regeneration of the distal segment of the nerve, while still remaining unconnected with the proximal segment, might, then, have been due to some influence received from the centres through these anastomotic fibres, or it might have received some influence from the periphery by terminal anastomosis with other nerves. Philipeaux and Vulpian, however, disposed of these objections by an experiment on the lingual nerve of a young dog. A portion was resected from the nerve, and the examination in forty-six days showed no reunion, fibres degenerated, and only feeble indications of restoration. For this examination a new portion had been excised, leaving a part of the lingual isolated both from the central and from the peripheral segments. At the end of thirty-eight days more, numerous new fibres were found, not only in the distal segment, but also in the section isolated from both ends; showing, thus, that regeneration is independent. Thus, these authors conclude that nerves, motor, sensory, or mixed, "separated from their centres may, remaining isolated from their centres, recover their normal structure and physiological properties"; and that nerve tissue has an autonomy as other tissues. Although the distal segment of the nerve can thus be completely restored anatomically and physiologically, while remaining separate from the centres, yet they found that reunion is not without its effects. Under the influence of reunion, the nerve is regenerated more rapidly than when remaining separate, but otherwise the character of the restoration is the same; and they hold that to regard this hastening of the restoration, as due to influence from the centres, can only be accepted as a provisional explanation of the facts, pending their true explanation. It is clear, however, that reunion, while not essential to regeneration of young nerve fibres, enables functional activity to be established and exercised at the earliest possible period, and, as it is well known in other tissues, that functional activity has an influence in promoting structural perfection, the same explanation may account for the rapidity of regeneration observed by Philipeaux and Vulpian, when reunion had occurred. These authors also describe the characters of degeneration and regeneration. They hold with Schiff that the axis-cylinder is retained, and that degeneration consists simply in a destruction and absorption of the myeline. The axis-cylinders remain, surrounded by their sheaths of Schwann, which support many nuclei, probably derived by proliferation from the nuclei of the sheath. Restitution is, then, simply a reaccumulation of the myeline, the new fibres having at first a small diameter, which gradually becomes greater, as the myeline accumulates. According to Philipeaux and Vulpian, then, degeneration is not a total destruction of the fibre, but simply an alteration; and reformation is a reaccumulation of the myeline, and is therefore not a true regeneration, but simply a restoration. In support of auto-genetic regeneration, they found, in a later investigation (47.), in two cases that portions of the lingual nerve, transplanted under the skin of the inguinal region in dogs, contained new fibres after six months

These results which, if true, are of so great importance in surgery, were so much against the view established by Waller, that they were not allowed to pass without severe criticism. While Brown-Séquard (40.) gave his assent, and later Cornil (48.)[x] supported from an experiment of his own, Schiff (41.), Landry (42.), and Ambrosoli (43.) wrote at the time opposing the opinions of Philipeaux and Vulpian, not only on the ground of their own researches, but also from a criticism of their work. Schiff pointed out that the animals upon which they had experimented were all very young, and that in the earlier periods of life, the nerves are less dependent on their centres in the cord and in the ganglia, and that

[x] Cornil, l.c., p. 97. "Ces conclusions" i.e. those of Philipeaux and Vulpian, "ont été parfaitment vérifiées dans plusieurs expériences instituées sur le même sujet par mon excellent maître M. Martin-Magron et moi. Sur un jeune chat albinos notamment, où la portion centrale du nerf facial coupé avait été arrachée jusque dans sa racine, nous avons vu, huit jours après l'opération, la dégénération du bout périphérique. Six mois après, nous avons constaté que l'électrisation de ce même segment nerveux produisait des contractions dans les muscles de la lèvre du même côté, et que les tubes de ce nerf avaient recouvré leur structure normale."

in the embryo they are so little dependent on the centres in the cord, that an embryo in which the cord had not developed, presented the anterior roots of the spinal nerves without pathological change. Ambrosoli explained the results on the same ground, and held that the nerves at an early period possess local nutritive centres; but both Schiff and Ambrosoli held that this independence only applied to the earliest periods of life, and that the results of Philipeaux and Vulpian could not have been obtained in adult animals. Almost all the subsequent writers have opposed the results of Philipeaux and Vulpian, some maintaining with Ranvier (102, Tom. II, 58), that the regeneration, which they found, was due to connecting strands between the two divided ends, which strands they had failed to observe; others that they had mistaken what they saw for regenerated fibres; and even Vulpian (77, 86) himself some years later, withdrew from his former position, admitted that what he had seen were not regenerated fibres, and denied the possibility of autogenetic regeneration of nerves

At this time, then, the general opinion was that degeneration of the whole peripheral segment resulted on separation of a nerve from its centres, and that regeneration only occurred on restoration of connection; but opinions differed on the parts of the nerve fibre affected by degeneration, Schiff (31,35), Philipeaux and Vulpian (39.), and Remak (49.) holding that the axis-cylinder remained; while Lent (34.) supported Waller (20,24) and Budge (21.) that it also disappeared. But the cases with speedy return of function observed by Paget (30), and experiments with a similar speedy return made by Schiff, could not be explained on the Wallerian doctrine of regeneration; and for these it was held that, in addition to the process of regeneration described by Waller, there must also be a more speedy mode of restoration — of healing by so called "first intention". But the term first intention, as applied to healing of divided nerves, implied more than the same term applied to other tissues. In both cases reunion occurs by the intervention of a minimum amount of new formed tissue, but in the former case, this would be of comparatively little avail for hastening the functional restitution of the nerve, if the process of regeneration described by Waller had to occur in the distal segment. It implied, then, that the distal segment of the nerve was retained in a condition fit to resume function immediately, or very soon after reunion had been established. Schiff's view that the axis-cylinder was retained made the explanation easy; for here the two ends of the axis-cylinders had simply to be connected; and on this ground Remak (49.), who also held that the axis-cylinder was retained, believed in the possibility of healing by first intention, although he had not himself observed it. But if the axis-cylinder also was destroyed, it was necessary to suppose that early reunion was able to arrest the progress or prevent the onset of degeneration; and this is the view which was taken by Paget, although not from direct observation.

The general opinion, however, was against the possibility of a reunion by first intention, when in 1864, the cases of nerve suture by Nélaton and Laugier were published. With the exception of a case by Baudens*, in 1836, of indirect suture of several of the nerves in the arm, which was not followed by favourable results by the eighth day, when the patient died from secondary hæmorrhage, these were the first

*After Létiévant (82.) p. 118

two cases of nerve suture in man published. Nélaton's case was published by Houel (54.) in 1864, but the operation was performed on 24th April, 1863, on a woman, aged 24 years, who had a neuroma on the median nerve, situated on the inner and upper part of the left arm. The neuroma was removed, and the ends of the nerve brought together with two sutures of silver wire passed through the nerve. At the end of the operation, the patient could move the fourth and fifth digits, but not the first, second, or third; and there was loss of sensation in the parts supplied by the median nerve.[x] On the fourth day, the sutures were removed on account of pain, and it was then determined that the patient could move the index and middle fingers slightly, but that opposition of the thumb was impossible. On the seventh day, function had been so much restored that she could move all the fingers, and oppose the thumb to the middle finger.

Laugier's (55) operation was performed on 13th June, 1864. The median had been completely divided, and the radial partially in

[x] The account of the condition of sensation immediately after the operation published by Houel was, according to Richet (62) p. 555, afterwards contradicted by Nélaton.

a wound, received the day before, on the forearm. Sensation was absent in the parts supplied by the median nerve, and the movement of opposition of the thumb was impossible. The median nerve was sutured with silk, passed through the ends of the nerve. On the evening of the day of operation, sensation was a little restored, the sense of touch being present, though obtuse. On the day following, tactile sensation had markedly improved, and the movement of opposition of the thumb was easy. In the next two days, the second and third after the operation, there was improvement in sensation and motion; but certain sensations were not perceived. Thus, there was no sensation of pain on pricking with a pin the palmar aspect of the middle finger; and the sensation of difference of temperature could not be distinguished. On the fourth day after the operation, the sensation of pain began to return obtusely, and temperature differences could be perceived. The case was published on the eighth day, when all the improvement gained had been conserved.

When these two cases were published, they gave rise to much discussion. The almost general opinion that to suture a nerve was to run grave risk of producing tetanus, neuritis, and other troubles, and the scanty details given in publishing the cases, induced several workers to begin investigations on animals, with the view of determining the effects of nerve suture. Eulenburg and Landois (56.) conducted seventeen experiments on rabbits and dogs, cutting the sciatic, and in other cases the vagus and sympathetic, and suturing with silk, horsehair, or metallic sutures. As a result of their work, they came to the conclusion that, even with perfect coaptation of the nerve and immobilisation of the limb, cut and sutured nerves show in rabbits and dogs no tendency to heal by first intention; that instead there was clear evidence of interrupted conductivity at the seat of suture, and loss of function; that the subsequent microscopical examination of the distal segment of the nerve, showed that it was degenerated, and that the axis-cylinder shared the fate of the myeline sheath; that in many cases neuritis and perineuritis, suppuration and metastatic processes in the lungs resulted from the employment of the suture; and, that with the want of details and of the later results in the cases of Nélaton and Laugier, the advisability of nerve suture in surgery was very problematical.

Guérin (57.) was also opposed to the use of sutures, as, in his opinion, it was a dangerous auxiliary. He was familiar with healing by first intention, and held that the nerve ends must be approximated, when the exudation of plastic material between the ends was all that was necessary for a functional reunion by the fourth or fifth day; but he was opposed to securing this approximation by means of suture.

Eulenburg and Landois (60.) in a further research corroborated their former conclusions, and added the further objection to the use of the suture, that it not only did not hasten, but actually hindered reunion. This conclusion they drew from an experiment, in which they had sutured the sciatic with iron wire. The foot became gangrenous, but the wound and gangrene both healed. Function did not return, although the animal lived for several months. On examining the seat of suture, they found the nerves united by a mass of connective tissue without any trace of nerve fibres.

The unfortunate results obtained by Eulenburg and Landois, which led them to declare against nerve suture, were in a measure counteracted by the work of Magnien (61.), published soon afterwards. From many cases of suture performed by him, in horses, rabbits, and cats, he was led to conclude that the suture in no way does injury; and in two cats he found after suture, return of sensation in seven and eleven days, and of motion in fifteen and twenty five days respectively.

In the following year attention was drawn to a fact, which seemed at the time inexplicable. The view that division of a nerve involved complete anaesthesia of the parts, supposed anatomically to be exclusively supplied by that nerve, was shown by Richet (62) to be not without its exceptions. A female, who had received a wound above the annular ligament at the wrist, was examined by him, and the median nerve was found divided. On cutting a portion from the distal segment, great pain was produced, and, moreover, the region of the skin supplied by the median nerve, still retained its sensibility; yet the muscles were paralysed. The nerve was sutured; but the operation does not seem to have been followed by return of function in the muscles. Lockhart Clarke (63), who saw the case eight days after the injury, testifies that the sense of touch was perfect, that the part touched was rightly localized, but that the sense of pain was dulled, and temperature sense unsatisfactory.

A similar case was published immediately afterwards by Kiallmark (64). The case was one in which the ulnar nerve had been divided at the elbow. A portion was cut off, producing thereby great pain, and this portion seemed to Kiallmark to include the whole thickness of the nerve. Yet beyond slight numbness in the little and ring fingers, the patient complained of no impairment of sensation or motion in the hand or forearm, and in a few days resumed his occupation.

Richet attempted to explain his case on the theory of recurrent sensibility, and also thus explained the return of sensation in Laugier's case, and asks, if the sensibility in that case was ever really absent. He also states that, contrary to the account of Nélaton's case published by Houel, Nélaton had told him that the sensibility remained after section, and before the suture had been applied.* But the cases remained more or less enigmatical, until the following year, when Arloing and Tripier (70.) made a series of experiments on dogs, with a view to explain the phenomena. For their purpose, they found the

*Richet, l.c., p. 555.

fore-limb of the dog most suitable. Their work was divided into two parts, first, the explanation of the sensibility remaining in the distal segment of a divided nerve, and second, the explanation of the sensibility in the skin after division of the nerve, which is supposed exclusively to supply it. They found, on examining by the Wallerian method, that after section of a nerve some fibres remained in the peripheral segment, which did not undergo degeneration; and to these was due the sensibility of the segment. They also found that, as long as one of the collateral nerves remained undivided, this sensibility was retained in a greater or less degree, provided that the section was made below the elbow. With regard to the sensibility of the skin, they found that it was impossible to find a part of the skin, which was exclusively supplied by a single nerve; that the section of one of the four collateral nerves supplying a toe, produced no change in the sensibility; that the section of two produced scarcely any loss of sensibility; that the section of three produced a more marked loss; and, that it required the section of all four to effect a total anæsthesia. They, therefore, concluded that the nerves supplying the paw formed by anastomosis a network in the skin, and that each papilla was supplied from all sources, and that some of the fibres of this network ascended the stems of the nerves, accounting for the undegenerated fibres seen microscopically, and for the recurrent sensibility. This explanation, then, was taken as accounting for the phenomena observed in cases such as that of Richet: the sensibility was there retained, owing to the neighbouring nerves also taking part in the supply of that part of the skin, which was apparently exclusively supplied by the median nerve.

In the following year a case was observed by Létiévant (73,82), which was unexplained by anything that was known at the time. The case was one in which for the treatment of tetanus, arising from a wound in the hand, he had divided the median in the upper third of the arm. He found, on examining a few hours after the operation, that not only did the sense of touch remain in the median distribution, but, although all the muscles supplied by the median were paralysed, there were present traces of movements resembling those performed by the paralysed muscles. After nine months, while the muscles supplied by the median were still paralysed and now atrophied, the movements were strongly developed. Thus flexion of the index and middle fingers, and flexion abduction and opposition of the thumb were all possible to a greater or less degree. On this case Létiévant founded his theory of "suppléances motrices et sensitives", a theory, which has since been taken to explain return of function after nerve section in many cases in which that return was really due to regeneration, with imperfect return of function. His theory is that neighbouring muscles take the place of the muscles which are paralysed, though necessarily in an imperfect degree. Thus, in his case, although the pronators were paralysed, still their function was imitated by the internal rotators of the humerus at the shoulder joint, coupled with the flexors of the forearm, the mechanical weight of the hand rendering the movement easier. The first phalanges were flexed by the interossei; the flexion of the second and terminal phalanges of the middle finger, by the tendinous expansion, which associates its flexion with that of the ring finger; while the second and terminal phalanges of the index, and terminal of the thumb were passively flexed by the extensors of the metacarpus, pulling on the paralysed flexor tendons; while the feeble opposition of the thumb was effected by the simultaneous contraction of the adductor and short flexor muscles. The retention of sensibility as far as touch is concerned, he explained as due to the finer anastomoses, and also to the sense of touch mediately communicated to neighbouring normal papillæ

But there have been several cases published, in which, after section of a nerve, although anæsthesia resulted after the section, and although it was concluded that reunion of the nerve had not occurred, yet sensibility returned in the course of time. Weir Mitchell (90.) published a case of this kind, in which for neuralgia he resected three quarters of an inch from the median in the forearm, and doubled up the ends to prevent reunion. Examined two weeks later, "there were large regions of the hand into which a needle could be thrust deeply without causing pain." The following year, he removed three inches from the musculo-spiral; and a portion of this nerve had three years before been resected, and regeneration had occurred. Some weeks after the second operation on the musculo-spiral, sensation returned in the median distribution, and there was also a notable retention of sensibility in the region supplied by the radial nerve. For this sensibility, according to Weir Mitchell, only some filaments of the internal cutaneous, of the musculo-cutaneous, and of the ulnar were responsible.

To account for such cases Tillmanns (123) suggests that from neighbouring intact nerves, filaments can grow out into the anæsthetic region, and instances the experience, which is met with in the plastic operation for repair of the nose from the tissue of the forehead, where for some time the patient refers the sensation of touch in the flap to the forehead, but ultimately rightly locates it. A more probable explanation of this phenomenon is, that sensation is conducted along twigs passing into the flap, which at first the patient refers to the forehead, as he has been accustomed to, but that he ultimately learns by experience to refer the sensation to the new position.

The explanation given by Remak (87.) to account for these cases with delay in return of sensation, and yet without reunion of the nerve, is that the anastomosing fibres may become developed, in a way comparable to the development of the collateral circulation after occlusion of an artery.

These theories, while they may be applicable, and doubtless are, to certain cases, have been made use of by some to account for early return of function after nerve section, when, in many of the cases to which these explanations are given, the return of function is really due to nerve regeneration. Indeed, Tillmanns and others refuse to take the return of sensibility at all as evidence of functional reunion of a divided nerve, unless that also is accompanied by return of voluntary muscular power. The view which many hold of the process of regeneration, involves for its accomplishment the lapse of a considerable period of time. Others, again, hold that, if the divided nerve is immediately sutured, it may heal by first intention, and function be restored speedily; but if this fails, the prolonged process of regeneration must occur. Yet, there are many cases published in which the process of healing by first intention has manifestly failed, and in which the return of sensibility occurs too soon for the process of regeneration usually accepted to have occurred. For these cases, the theories which have been described are taken as an explanation. Thus Vanlair (122), who holds that, if first intention can occur, it is at most very exceptional, holds that, if sensibility returns very soon after nerve section, it is due to anastomosis, and the anæsthesia present for the short interval has been due to the numbing effects of hæmorrhage; if more slowly, it is due to supplementary fibres; and, if there is a very long delay before restoration of function, then it is due to regeneration.

The histology of degeneration and regeneration of nerves has been so frequently investigated, that from the time of Waller, scarcely a year has passed without the appearance of one or more papers upon the subject. Most of these investigations have been conducted on rabbits, fowls, guinea pigs, dogs, cats, and rats. On some of the questions almost all are in agreement; while on others there is great diversity of opinion. All authors agree with Waller that the ultimate result of separation of a nerve from its centres, is degeneration of the part separated, but, in opposition to the majority who regard this degeneration as inevitable, Schiff (31, 35.), Bruch (32.), Guérin (57.), Hertz (72.), Gluck (98.), and Wolberg (117, 127) believe that, if the divided ends are accurately coapted, and reunite before degeneration occurs, healing by first intention takes place, and the degenerative process is avoided. All are also agreed since the work of Schiff and that of Lent (34.), that preceding the Wallerian degeneration, there is a traumatic degeneration affecting a small portion of the central and peripheral ends. Much diversity of opinion, however, exists as to the nature of degeneration, and the parts of the nerve fibre which it affects. The older writers Nasse (15.), Schiff (31.), Landry (42.), Walter (46.), and others describe the change as simply a fatty degeneration, the resulting fat being simply absorbed. Bruch (32.), again, regards it as a coagulation, comparable to that which takes place after death, but ultimately becoming fatty. Ranvier (79.102) regards it as caused by the increase in the nucleus and protoplasm of the interannular segment, which first cuts the contents of the fibre into two in the middle of the segment, and ultimately breaks them up into segments by the increase of the protoplasm lying in the indentations of Schmidt (85.) Meanwhile, the myeline breaks into an albuminous and fatty constituent, and is gradually absorbed under the influence of the increasing protoplasm. Howell and Huber (154.) find that the process begins as a coagulation, and that the myeline breaks into the segments of Lantermann (92.) before the increase of protoplasm commences. The further fragmentation and absorption is brought about under the influence of protoplasmic increase, but a fatty element is not found. Colasanti (106) and Tizzoni (107) regard it as in the first instance a breaking up into the segments of Lantermann; and the latter holds along with Korybutt-Daszkiewicz (103.) that the further destruction takes place by means of leucocytes, which have wandered into the interior of the fibre by diapedesis, through openings in the sheath of Schwann, or at the cut end. Ranvier, it may be mentioned, describes the entrance of leucocytes into the fibres of the central and distal ends under the influence of which, the myeline sheath is broken up; but he holds this view only for the traumatic degeneration, and maintains that in the paralytic degeneration of the distal segment, they have nothing to do. Stroebe (156) holds that the contents of the tube break up into irregular masses, which are partly fatty, and that the corpuscles formed by proliferation of the nuclei of the sheath of Schwann and the protoplasm, act towards the degenerated contents as phagocytes, transporting them into the lymphatic system. Büngner (150.) and Notthafft (157.) regard the shrinkage of the axiscylinder as the cause of the first fragmentation of the contents of the tube, and the increase of the interannular protoplasm and nuclei as the cause of the further breaking up and absorption. Neumann (68, 112.) Eichhorst (83.) and Dobbert take a different view from any other authors, namely, that the change after section is not a true degeneration, but a chemical alteration both of the myeline and of the axis-cylinder, whereby the difference between these two disappears, and the sheath of Schwann is filled with homogeneous protoplasmic contents, nothing being absorbed. This view they take from the different reaction to osmic acid, of the contents of the tubes, at various stages of degeneration. They find, as others have found, that the bluish black stain characteristic of myeline, gradually changes, and becomes less intense, until the colour is a uniform greenish yellow, and this they take as indicating not a replacement, but a gradual change of the contents to protoplasm. They also think that their theory is favoured by the fact that the sheaths of Schwann at the ultimate stage of change, are in transverse section circular, and not collapsed as they would be if empty.

Opinions are divided on the parts of the nerve fibre which degenerate. The view taken by Waller (20, 22, 24) that the whole of the fibre degenerates, namely, that the axis-cylinder and myeline sheath are broken up and absorbed, and that the sheath of Schwann becomes simply a string of connective tissue, is supported by Walter (46), Landry (42.), Ambrosoli (43.), Eulenburg and Landois (56.), and Vanlair (122). Also Benecke (78.), Bertolet (90), Bakowiecki (94), Cornil (119), Ranvier (102), and, recently, Büngner (150), Howell and Huber (154), Stroebe (156), and Notthafft (157) hold to the same view, but modified in so far that, while the axis-cylinder and myeline sheath are early destroyed and absorbed, the sheath of Schwann remains until it is disposed of, to make room for the growth of the young regenerated fibres. The view maintained by Lent (34), Rindfleisch (88.), Colasanti (106), Aufrecht (104), Tizzoni (107), Leegaard (116), Falkenheim (118), and Peyrani (128) is that the axis-cylinder and the myeline sheath are destroyed and removed, and that the sheath of Schwann persists. Hertz (72) takes the same view, except for the cases where healing by first intention occurs; and Erb (84.) that in slight injuries such as compression, the axis-cylinder is retained, but that where there is complete division, it is destroyed, but only at a late period, and that even then it may be of importance for regeneration. Vulpian (77.), also, in his later work, finds that the axis-cylinder disappears. Ranvier (102) holds that in the traumatic degeneration of the central end, the axis-cylinder is only exceptionally destroyed.

That the myeline sheath is destroyed, while the axis-cylinder and sheath of Schwann are retained, is the view advanced by Schiff (31, 35), Philipeaux and Vulpian (39), Hjelt (44.), Magnien (61), Laveran (67.), Hertz (72.) (for cases where first intention occurs), Erb (84.) (for slight injuries), Gluck (98.), Mitchell (80.), and Wolberg (127.); while Korybutt-Daszkiewicz (103.) holds that the axis-cylinder is broken up, but retained; and Remak (49) believes also that it is retained not from direct observation, but on the ground that he found that it belongs to the most resisting structures of the body, resisting putrefaction longer than bone.

The increase in the number of the nuclei of the sheath of Schwann during the process of degeneration, has been observed by all, but the phenomenon has been differently interpreted. Schiff (31.), Lent (34.), and Wolberg (127) state that the increase in number is only apparent, that it is not due to multiplication, but to the removal of the myeline, which previously hid the nuclei now visible. With these exceptions, the authors generally believe that the increase in numbers is real, and most believe that it is due to proliferation from the preexisting nucleus of the interannular segment. There is, however, difference of opinion on the import of this proliferation. Eichhorst (83.) gives as his opinion that the nuclei have nothing to do with regeneration, without giving an opinion on their destination. Ranvier (79, 102) and others think that the multiplication of the nuclei and protoplasm is the active agent in bringing about the destruction of the myeline sheath and axis-cylinder by compression; Stroebe (156.), that they act in part as phagocytes to the myeline and axis-cylinder. Howell and Huber (154), Stroebe (156), and Notthafft (157.) think that they take a subsidiary part in regeneration; while Hertz (72.), Benecke (78.), Bertolet (90.), Aufrecht (104), Leegaard (116), Bowlby (146.), and Büngner (150) take them as of the first importance in the regenerative process.

Friedländer and Krause (133.) in 1886, recorded their dissent to the generally accepted view that the central segment, with the exception of a very small portion at the cut surface, remains normal after section of a nerve. While admitting the degeneration of the peripheral segment, they hold that the central segment does not remain free from change. They made their observations on the nerves in the stump after amputation, and found that the transverse sections of such nerves do not present a normal aspect, but show a special form of degeneration, which they prefer to call atrophy. They found that about one half of the nerve fibres are without myeline, and present in transverse section a point in their centre, which may be the axis-cylinder, but which they think is doubtful. These atrophic fibres are only about one third the diameter of normal fibres. They then found that the anterior roots were normal, while the posterior contained principally fibres of this atrophic character. They hold, then, that in the central segment after division, the sensory fibres undergo this form of degeneration, while the motor remain normal. But all the sensory fibres do not so atrophy, and they give the hypothesis that it is only those ending in the tactile corpuscles of Wagner and Meissner and in the end bulbs, which atrophy, while the fibres with free endings remain normal. In estimating the value of their work, it is well to remember that with the exception of one case which was three months after the amputation, and in which the atrophy was not so distinct, all the nerves which they examined, were from stumps of long standing, namely, from three to ten years.

Krause (136) in the following year published further investigations on the same subject. He examined human nerves from limbs, which had been amputated for gangrene. The gangrene he takes as equivalent to section of the nerve, and the portion of nerve above the gangrene, as equivalent to the central segment. He found, then, that examining such nerves three to four weeks after the onset of the gangrene, about one half of the fibres were in a state of degeneration, not to be distinguished from the degeneration of the distal segment after nerve section. Both the axis-cylinder and the myeline sheath were affected, and traces of myeline were left, and there was proliferation of the nuclei of the sheath of Schwann; and he found that it was a centripetal degeneration. He then examined the distal segment of divided nerves in the rabbit, and recognised the few sound fibres, which many had seen before and attributed to the recurrent fibres, and in the central segment he recognised a corresponding number of degenerated fibres. From this, seeing that one half of the fibres degenerate in the central segment of the human nerve, he concludes that a similar number remain sound in the human distal segment; but he has not been able to verify this point. He puts forward the hypothesis that those fibres which degenerate in the central segment, and which, by analogy, he concludes remain normal in the peripheral segment, have their nutritive centres in the periphery; and these he thinks most likely situated in the touch corpuscles, which Wagner and Meissner showed to exist only in man and monkeys; and from the absence of these touch corpuscles he seeks to explain, why in the rabbit and other animals so few fibres degenerate in the central segment, and remain normal in the peripheral. He concludes that in the central segment degenerate, and in the peripheral remain intact, all those sensory fibres which are in connection with a trophic centre in the periphery, and that in the central segment remain intact, and in the peripheral degenerate, all motor fibres, and the sensory fibres of the bones, periosteum, joints, muscles, tendons, fasciæ, and, of the cutaneous nerves, those ending free in the skin. He explains on his theory how sensation may return after nerve section without return of motor power, as this is caused by a centripetal growth of the distal segment, which forms attachment to other nerves.

The period at which the degenerative changes begin is of great importance in the consideration of the possibility of reunion by first intention. While the traumatic degeneration of the cut ends occurs within a few hours, the paralytic degeneration does not show until the lapse of a longer period of time. This period has been variously given by different authors, and this discrepancy is explained by Ranvier (102), who shows that it is different for different species of animals. Thus he found that taking the physiological test of loss of conductivity to electrical stimuli, in the rabbit, guinea pig, and rat conductivity was lost in forty-eight hours from the time of section, while it was retained in the dog, pigeon, and frog; in seventy-two hours it was lost in the pigeon, and retained in the dog and frog; in four days it was lost in the dog and retained in the frog; and, that it was retained in the frog for thirty days or longer. Also, the age and state of the animal caused variations. But these data refer to the stage in degeneration at which function is destroyed, the actual onset of degeneration being much earlier. Thus, in the rabbit according to Ranvier, the changes are in progress by twenty four hours.

The authors who have published accounts of regeneration of nerves, hold even more diverse opinions than are held concerning degeneration. The view which is held by the minority of original investigators, but which is the account most usually given in text-books, since the investigations of Ranvier, is that regeneration of the distal segment is effected entirely from the end of the central segment. According to Ranvier (102), the distal segment still contains the sheaths of Schwann, after degeneration and absorption of their normal contents. Reunion occurs between the proximal and distal ends, at first by means of granulation tissue. In the first days while degeneration is proceeding, the axis-cylinders of the central end swell up, and appear slightly bulbous, most of the axis-cylinders being retained in the region attacked by traumatic degeneration. These central axis-cylinders show a longitudinal striation, which Ranvier takes as equivalent to the fibrils of Schultze, and from each old axis-cylinder sometimes one or two new axis-cylinders proceed, sometimes many, as if the old axis-cylinder had split into its primitive fibrils. These continue their growth as far as the old sheath of Schwann extends, that is to the cut surface, and then pass into the cicatricial tissue. They pass across this, and some of the new axis-cylinders then pass into the interior of the old sheaths of Schwann of the distal segment, while others pass between them, and run in the endoneurial tissue. The new axis-cylinders continue to advance, till they reach the end organs. Meanwhile, the new axis-cylinder becomes clothed with its sheaths; and the new sheath of Schwann is distinguished at first by the shortness of its internodes. Often several new fibres are contained in one old sheath of Schwann, which is thereby greatly distended, and ultimately destroyed. At times the new fibre after leaving the old axis-cylinder divides, and the branches may again give off branches. Thus, the distal segment acts merely as a guide to the developing new fibres, playing an entirely passive part in the work of regeneration. Ranvier is therefore at one with Waller (23.), except that the former finds that the new fibres penetrate into the old sheaths of Schwann, as well as between them. Rindfleisch (88.) gives the same account, with the difference that the old sheath of Schwann is retained for the new fibre. Vanlair (122) believes that the new fibres never penetrate into the old sheaths of Schwann; and, moreover, he regards the distal segment as resisting the growth of the new fibres to the end organs, and even suggests the excision of the whole distal segment, leaving the connective tissue sheath, as a means of leaving the path clear for the passage of the new fibres, and hastening the progress of regeneration×. He finds that the new fibres at the time of their branching from the old are naked axis-cylinders; that they become clothed by a provisional sheath (gaîne vitreuse), derived from the neighbouring connective tissue; that this becomes thinner as development proceeds, and between it and the axis-cylinder, the myeline sheath and new sheath of Schwann appears, while the provisional sheath becomes the fibrillar sheath. He finds, also, that maturation of the fibre occurs centripetally. In a later investigation, Vanlair (158) has sought to discover

×Vanlair (122) p. 485.

the rate at which the growth of the new fibres occurs, and found that for the facial nerve it was at the rate of 0·3 mm. daily, and for the vagus and sciatic that of 1 mm. daily, both in the case of simple section with perfect coaptation. Recently Howell and Huber (154) have decided in favour of this process of regeneration, but their observations have led them to accord the distal segment a greater share in the work of regeneration. They find that the protoplasm and nuclei of the sheath of Schwann, in that portion of the nerve, form spindle cells which unite so as to form protoplasmic threads, running within the old sheath of Schwann. These they term "embryonic fibres", and find that while they have no axis-cylinder, they possess a low degree of irritability and conductivity. These are formed even when the peripheral has no connection with the central segment; but they are not true nerve fibres. The latter are formed by axis-cylinders, which grow out from the axis-cylinders of the central segment, and insinuate themselves into the centres of the embryonic fibres. The latter develop the sheaths around the axis-cylinders. Stroebe (156) also finds growth from the central segment as forming only the axis-cylinders, which penetrate either into the old sheaths of Schwann or between, and become clothed with new sheaths from the cellular elements of the distal segment; and Notthafft (157) thinks that the new sheaths of Schwann are probably derived from the cells of the old.

The advocates of the view that the distal segment has an independent regeneration of nerve fibres, differ in their views regarding the mode of origin of these fibres. Those who believe that the axis-cylinder is retained during degeneration, point to that structure as the source of the new fibres. Thus Schiff (31.), Philipeaux and Vulpian (39.), Hjelt (44.), and Wolberg (127) believe that regeneration in the distal segment is simply a reaccumulation of the myeline, and Laveran (67.) thinks that the myeline is secreted by the nuclei of the sheath of Schwann. Korybutt-Daszkiewicz (103) regards the remains of the old axis-cylinder as the source of the new. Remak (49.), who observed as many as ten to fifteen small fibres enclosed in one old sheath of Schwann, regards them as having originated from the old axis-cylinder by longitudinal splitting.

This, however, only refers to the distal segment, and these authors have to account for the formation of new nerve fibres in the cicatricial mass uniting the cut surfaces. Hjelt, Wolberg, and Hanken (143.) derive the new fibres here from the nucleated corpuscles of the perineurium. Laveran supposes that the intercalary segment is bridged over by outgrowth of axis-cylinders from the central end, and these find their envelopes from organised leucocytes; while Gluck(98) finds that the tissue formed between the ends is a specific granulation tissue, capable of conducting impulses and forming spindle cells, which unite end to end to form young fibres, which bridge over the gap.

Neumann (68, 112) and his pupils Eichhorst (83) and Dobbert, who describe degeneration as a chemical change in the contents of the fibre, find that regeneration is a reproduction of the chemical differentiation between the axis-cylinder and the myeline sheath, but in this reproduction more than one fibre may be produced in one old sheath of Schwann. A new sheath of Schwann is formed around each new fibre, and the old dis-appears or becomes part of the endoneurial tissue. Neumann holds that the new fibres thus formed bridge over the cicatricial interval by growth both from the central and from the peripheral ends, and Eichhorst, that this is effected only from the central end.

Those who believe that the axis-cylinder is destroyed in degeneration, hold different opinions on the mode of origin of the young fibres. Hertz (72) thinks that in some cases, they are formed from the white blood corpuscles, which become spindle shaped and unite by processes. Bruns (74.) derives them from the corpuscles of the connective tissue of the nerve; and Hochwart,(142) from the connective tissue corpuscle, or from the nuclei of the old sheath of Schwann, which nuclei he regards as originally derived from the connective tissue corpuscle. But the nuclei of the sheath of Schwann have been taken by the majority, as the source of the regenerated fibre. At first, before the relationship between the nuclei and the protoplasm of the sheath was understood, the nuclei themselves were taken as the source, but more recently the principal rôle has been given to the protoplasm. Hertz (72.) finds that the new fibres are sometimes formed from these nuclei, which are surrounded with protoplasm. They become spindles, unite end to end, and form fibres. The outer part differentiates a myeline sheath and sheath of Schwann, while the central part remains as the axis-cylinder; and during the process many of the nuclei disappear, and the remainder become the nuclei of the new sheath of Schwann. Benecke (78.) gives a similar account, and attributes to the nuclei the secretion of the myeline sheath which appears around them, while many of the nuclei disappear. Bertolet (90.), Aufrecht (104.), Leegaard (116.), and, recently, Büngner (150) have all advocated the same view, the latter having described the process in detail, after an extended series of researches. Thus, he traced the development of the young fibres, lying within the old sheath of Schwann, from fusions of spindles derived in this way. The young fibre shows longitudinal striation, the beginning of the axis-cylinder. The new myeline sheath is formed from the outer layer of the young fibre, and also partly by absorption of the remains of the old myeline. The old sheath of Schwann disappears, and he regards the new as derived from the endoneurial connective tissue. The nuclei of the new sheath of Schwann are the direct descendents of the nuclei of the old sheath of Schwann, and have clearly the value of neuroblasts. The cicatrical tract is bridged over by extension of these neuroblasts into it.

Thus the different views on the process of regeneration may be grouped under two heads.

1st The new fibres of the peripheral segment are produced exclusively from the central end by centrifugal growth.

2nd The new fibres originate in the peripheral segment, and become connected to those of the central end.

According to the first view, the process of regeneration requires for its accomplishment the lapse of a more or less long period of time, depending on the length of the distal segment;

while, according to the second view, the time required is not necessarily long, seeing that the material for the work of regeneration is already laid down along the whole length of the distal segment.

That which has probably gone far to support the view taken by Ranvier, is the evidence of histogenesis of nerves. Kölliker (109) gave the opinion that the peripheral nerves were produced by outgrowth from the central nervous system, and that these outgrowths were not cellular, but consisted from the first of bundles of axis-cylinders. The sheaths of the axis-cylinders were formed later from the mesoblastic elements through which the axis-cylinders passed. His (111. 144. 147.) also supports the view that at their first appearance the nerves are not cellular, but bundles of fibres, and these he regards as processes from the neuroblasts. Thus, an axis-cylinder is a cell process, the cell lying in the cord or spinal ganglion, and, therefore, when cut across in any part of its course, the amputated cell process must necessarily die, having no independent life; and its place can only be taken by the stump continuing its growth, as it did in the embryo. But in opposition to Kölliker and His, the examination of the origin of the spinal nerves in the dogfish and chick, led Balfour (93, 121.) and Milnes Marshall (97.), while corroborating the epiblastic origin of nerves, to maintain that at their first appearance from the sides of the cord, the nerves are cellular. Balfour says[*] "the cellular structure of embryonic nerves is a point on which I should have anticipated that a difference of opinion was impossible,...... As the nerve fibres become differentiated from the primitive spindle-shaped cells, the nuclei become relatively more sparse, and this fact has probably misled Kölliker." He found that the anterior roots grow rapidly, and soon form elongated cords of spindle shaped cells from which the nerve fibres are differentiated. This view, then, is in accord with the view of regeneration taken by those who believe that it is effected from cellular elements in the distal segment. These epiblastic cellular elements proceed to form new fibres by becoming spindle shaped, and uniting end to end, in the same way in which Balfour found the cellular elements develop in the formation of the nerves in the embryo. Korybutt-Daszkiewicz (105.) has seen in frogs a formation of nerve fibres in a way which accords with this view. The frogs were starved for a time, and then placed in favourable surroundings,

[*] Balfour (121.) Vol. ii, p. 372

and well nourished. On examining the nerves, plasma cells were found, which examined at different periods, were found to elongate and unite with each other and form nerve fibres.

Many of the cases of secondary suture published speak strongly against the slow process of regeneration from the central end. One of the first of these was a case published by Jessop (75.), where the ulnar nerve had been cut across above the wrist nine years before the operation of suture. Before the operation there was total loss of sensation and motion in the region supplied by the ulnar. The hand was thin and the palm hollowed out. The cicatrix uniting the ends was excised and the nerve sutured, and eight days after the operation sensation began to return, and in eight days more had returned everywhere except at the tips of the fingers. A similar case was published by v. Langenbeck.* In his case the sciatic had been cut across two and a half years before the operation, and there was total anæsthesia; and yet sensation began to return three days after the operation. Also Ogston (120.) performed secondary suture of the ulnar in a case in which the nerve had been cut long enough to

*After Wolberg (127) p. 341.

produce the characteristic atrophy and claw-hand, and in which there was total loss of sensation and motion; and yet, a week after the operation the return of sensation was determined.

Many similar cases have been published, and although return of sensation after section has been explained by theories of anastomosis and supplementary supply, yet no such theories can explain the course of events in these cases. For, although a case of primary suture in which after operation sensation returns and not motion, may be explained as due to supplementary sensory supply, yet the relationship in these cases of secondary suture between the operation and the return of sensation is such that the return of function must be regarded as the result of the reunion of the nerve. In these cases sensation remained absent until the operation of suture was performed, and it cannot be supposed that the supplementary nerve supply made its appearance by coincidence, at the time of the secondary suture. Indeed, Vanlair (122.) regards such cases as inexplicable by the theory of regeneration which he supports.

Part II.

My own observations were made on four cases, in three of which the nerves had been accidentally divided some time previously, and functional reunion had not occurred; while in one the nerves were functionally interrupted by compression at the seat of a fracture. The cases were as follows:—

Case I. Division of the ulnar and median nerves in the forearm.

Case II. Division of the median nerve in the forearm.

Case III. Interruption of the median, ulnar, and musculo-spiral nerves, resulting from a fracture at the elbow joint.

Case IV. Division of the ulnar nerve in the forearm.

These cases, therefore, presented seven injured nerves. In the cases of division, I performed the operation of secondary suture, and in that of compression at the seat of fracture, dissected the nerves from their adhesions, and removed the compressed portions from the median and musculo-spiral, and sutured. In every case the portions removed were preserved for microscopical study.

Case I (Plates II and III)

A boy, aged 16 years, received a wound with a piece of glass, on the front of the right fore-arm in its middle third. The wound was deep, and bled freely. It was sutured, and healed in about eight weeks, but by that time it was apparent that damage had been done to the nerves, as the hand was paralysed and sensation lost. Soon atrophy manifested itself, and the boy was unable to return to his work. He came for advice on 3rd March, 1894, fully six months after the accident, and his condition was found to be as follows. A cicatrix four and three quarters inches in length, extended across the middle third of the front of the right fore-arm, obliquely from above downwards and in-wards, crossing almost the entire breadth of the forearm. The lower and inner third of this cicatrix was red, and painful when firmly pressed; the middle third was extremely red, and prominent at its junction with the inner third, and its surface was thin and very tender even to the slighest touch; the upper and outer third had the appearance of an ordinary cicatrix. On moving the fingers, the cicatrix was found adherent to the muscles. The muscles of the forearm were atrophied, the right forearm being everywhere a quarter of an inch less in circumference than the left at corresponding levels.

The trophic changes in the hand were well established. The skin was smooth, red, and shining, and the flexures but little marked. There was a raw surface without signs of healing, on the inner side of the first internode of the fifth digit; and this was the result of a burn received two weeks previously. The nails had a corrugated surface. The hand was colder than the left. There was great atrophy of the small muscles, the palm being hollowed out, and the thenar and hypothenar eminences replaced by hollows.

The attitude and movements of the hand were those characteristic of section of the median and ulnar nerves. Thus all the fingers were held flexed at the two interphalangeal, and overextended at the metacarpo-phalangeal joints. The fingers could be passively extended, but voluntarily only to a slight extent, and in both cases only with accompanying flexion of the hand at the wrist. The hand was carried semi-flexed at the wrist simulating wrist-drop, but could be voluntarily straightened, although it could not long be held in that position, as a painful feeling was soon developed. He could also perform lateral movements of the hand at the wrist. The hand could only be partially closed, and when he attempted to extend his fingers keeping the wrist straight, only the first phalanges responded, the two distal remaining flexed. The movements of adduction and opposition of the thumb, and abduction of the fingers were impossible. With the hand dynamometer he registered with the right hand 4 kilos., and with the left, 16 kilos. The small muscles of the hand tested electrically gave no response to the faradic current, but responded to the galvanic current.

The condition of sensation was as follows. There was pain elicited by pressure over the terminal phalanx of the thumb; absolute anæsthesia even for touch in every part of the fifth and fourth digits; very slight sensation, but none for pain, as tested by pricking the skin with a pin, on the third digit and palmar aspects of the second and first; total anæsthesia of the palm and of the ulnar side of the dorsum of the hand; and normal sensation on the radial side of the dorsum of the hand, and over the thenar eminence and dorsal aspects of the first and second digits.

On 15th March, 1894, exactly six and a half months after the accident, I performed the operation of secondary suture. The median nerve was laid bare at the seat of section, and the two ends of the nerve were found united by a dense cicatricial mass, somewhat thicker than the nerve, and about half an inch in length. This cicatricial mass lay under the middle third of the skin cicatrix, which was found at the examination to be so very tender. The nerve itself was much thicker than a normal median nerve.

The ulnar nerve was next exposed through the same incision. It was found similarly hypertrophied, but the ends were separated about three quarters of an inch. The central end lay about the level of the tender inner and lower third of the cutaneous cicatrix, and presented a hard bulb, measuring about half an inch in length and three eighths of an inch in transverse diameter. The peripheral end lay at a lower level than the cicatrix in the skin, was not so much hypertrophied, and presented a bulb about half the size of that on the central end. It lay surrounded by loose connective tissue.

The cicatrix on the median was excised at its junction with the ends of the nerve and while the surface exposed at the central end, showed nerve substance, that on the peripheral presented a homogeneous aspect. On removing an additional slice from the latter, nerve substance was exposed, and the section presented an appearance similar to that of the central end. The bulb on the central end of the ulnar was then cut off, and then the smaller bulb from the peripheral end, the sections in both cases exposing nerve tissue. Two sutures of chromic catgut were passed through each of the nerve ends, by means of a flat needle, the plane of the needle being kept parallel to the course of the nerve fibres, in order to inflict as little damage as possible. The hand and forearm were then fully flexed, and the sutures tied. The median came together easily, but the ulnar ends could not be brought together nearer than a quarter of an inch. The forearm and hand were then fixed fully flexed in a splint.

Three days after the operation, the first sign of returning sensation appeared; for on pinching the tip of the little finger, while the patient's head was covered, he cried out with pain. On the following day, he recognised the little finger when touched, and felt pain when it was firmly grasped or pricked with a pin. On the ninth day the wound was dressed for the first time, and the patient stated that he felt his hand much stronger than before the operation. The improvement in sensation was maintained. On the nineteenth day relaxation of the extreme flexion was begun gradually, and a more careful examination made of the condition of sensation. It was then found that he localized correctly all parts of the fingers touched, unless when the touches were slight, when he occasionally mistook the finger touched, and occasionally failed to feel gentle touch on the little finger. The sore on the first internode of the little finger was now quite healed, and the operation wound was healed, unless the extreme ends through which drainage had been made. Towards the end of the first month the sensation had still further improved; for now he located correctly the gentlest touches, and responded quicker than he did at first. The limb had now been gradually extended, and the fingers also had now been fully extended by firm bundaging to the splint. He could also at this time partially close and again open the hand. Electrical treatment of the hand was then commenced. With the positive pole applied above the wrist over the respective nerves, and the negative to Ziemssen's points over the small muscles, there were no contractions with the faradic current, but with a moderate galvanic current, there were distinct contractions of the small muscles of the thumb; but only very slight contractions could be detected in the other small muscles. By a month and a half from the date of operation, the electrical condition had improved; for now while all the small muscles responded to the galvanic current, the small muscles of the thumb gave contractions with the faradic current. There was also a notable return of power in the hand, as his grasp was appreciable. He was able to write legibly; which he was quite unable to do before the operation. By two months, the appearance of the skin had improved, and he was able to open and close the hand; but beyond a slight degree he could not oppose the thumb. The cicatrix of the original wound which was so red and tender before the operation, had now the appearance of an ordinary cicatrix, and had lost its tenderness. In the fifth month, he stated that he found no difference in sensation between the two hands, and that the hand was useful, although he was still unable to perform the more delicate movements; and this was explained by the persistent weakness of the opponens pollicis muscle. Despite the improvement in power, the atrophy of the palm and of the thenar and hypothenar eminences was still distinct, though less. This patient was last seen seven months after the operation, and at that time the improvement in sensation and motion was maintained, and the grasp of the hand much stronger. The sensation of the hand was perfect, and the appearance of the skin much improved; but there was still marked atrophy of the small muscles. The improvement in grasp up to that time is shown in the following table, taken with the hand dynamometer.

Date.		Right.	Left.
March 3rd	Before operation.	4 kilos.	16 kilos.
March 15th	Date of Operation		
May 1st		2 "	
May 8th		4 "	
May 16th		7 "	
June 21st		8 "	16 "
October 19th		14 "	29 "

Case II

A man, 37 years of age, a carpenter, on 20th November, 1894, received a deep wound with a chisel on the right forearm, transversely, just above the wrist in front. The wound was not stitched, and was said to have healed in about a fortnight without suppuration. Immediately after the accident, he noticed loss of sensation in the thumb, index, and middle fingers. Sensation did not return, and the hand being useless, he sought advice on 28th February, 1895. His condition then, three months and eight days after the accident was as follows.

On the right forearm there was a linear cicatrix, one inch in length, situated transversely above the wrist in front. Through this cicatrix a dense oval swelling, about the size of an almond could be felt in the middle line of the forearm, and on applying pressure a tingling sensation shot up the arm, and down into the hand. The skin, especially of the front of the index finger, thumb, and outer half of the palm was smoother than is natural, and the flexures were greatly diminished. There was marked atrophy of the thenar eminence. The index and middle fingers could not be fully extended, nor could they be brought into contact with the palm; and there was considerable loss of power of flexion of the thumb, and the movement of opposition was impossible.

The condition of sensation was the following:– total anæsthesia on the anterior aspects of the thumb, index and middle fingers, and on the outer half of the palm; only obtuse tactile sensation on the outer side of the ring finger and over the thenar eminence. On pricking with a pin the palmar surfaces of the thumb, index, middle, and outer half of the ring fingers, no pain or other sensation was felt.

On 28th February the median nerve was exposed by a longitudinal incision two inches in length over the seat of injury. The nerve was found hypertrophied, and the ends united by a dense mass of cicatricial tissue, about three quarters of an inch in length, and half an inch in greatest breadth, but flattened antero-posteriorly. This mass was excised at its junction with the nerve, and the sections exposed at the ends of the nerve showed points of what appeared to be nerve substance, but these were separated by dense white tissue. Two sutures of chromic catgut were passed through the whole thickness of the nerve, and the ends drawn together; and this was easily effected, when the hand was fully flexed. The wound was closed, and no drainage used, and the limb bandaged to a splint with the hand fully flexed.

Two days after the operation sensation commenced to return. The sense of touch was present on the palmar aspects of the fingers and thumb, and a pin thrust into the palmar aspect of the thumb was felt as a painful sensation. But sensation was still vague. By the ninth day sensation was much improved, and by the thirteenth day pain was felt from the prick of a pin in the palmar aspects of all the affected fingers and in the thumb, and by the seventeenth day, there was still further improvement. From this time the hand was gradually relaxed, and, finally, about the fourth week when got into the extended position, the splint was discarded. A fortnight later there was distinct improvement in the muscular power of the hand. Towards the end of the second month (24th May) his sensation had further improved, and both touch and sense of pain were quite distinct, although not yet felt by the patient so distinct as in the other hand, but the point of the index finger was not so sensitive as the other parts of the median distribution. The improvement in the muscles was very decided; for not only had the atrophy of the thenar eminence in great part disappeared, but the movement of opposition was now so well developed, that he was able to touch the tip of the middle finger with the tip of the thumb. At the end of six months, there was still further progress. Location of touch was perfect for all the parts concerned, and there was much improvement in the sensation of the last phalanx of the index finger; but even yet the patient found sensation less acute than in the sound hand. The grasp was almost as good as that of the left hand, and the movement of opposition was still further improved, since now he could touch with the thumb the tip of the ring finger. What prevented him from having as perfect use of his hand as formerly, was his inability to flex completely the terminal phalanges of the index and middle fingers. Thus, when he closed his hand, the tips of these fingers did not come sufficiently into the centre of the palm to enable him to grasp firmly smaller objects; but for larger objects his grasp was as firm as that of any average hand. He had already some time since returned to his work, being able to use his hand. At the end of nine months the condition was further improved. He could distinguish with each finger the difference between the smooth and rough side of sand paper. The atrophy of the thenar eminence had not only disappeared, but the eminence was even slightly greater than that of the left hand, and he was able to pick up the smallest piece of paper between fingers and thumb, although at six months he could only pick up a coin. At the end of a year, there was still further improvement, as he could now oppose the thumb to the little finger, but the grasp for smaller objects was still defective from his inability to flex completely the terminal phalanges of the index and middle fingers, although it was better than at nine months. His sensations of touch, pain, and thermic difference were correct, although not felt quite so clearly as in the left hand. As showing the degree to which the grasp had improved compared with that of the left hand, the dynamometer reading is of importance. One year and four months after the operation, with the right hand he registered 54 kilos., and with the left 58 kilos. (Plates IV and V).

Case III (Plates VI and VII.)

A girl, aged 6 years, sustained a fracture of the left elbow joint from a fall. The limb was fixed in splints, which were removed at the end of four weeks. Her hand was then found to be anæsthetic and paralysed. On 12th Dec., 1895, eight weeks after the accident, I first saw her, and found her condition to be as follows.

The internal condyle at the elbow joint was thickened, but otherwise the appearance of the joint was normal. The joint, however, only permitted a slight range of voluntary movement, and even under chloroform this range could not be much increased on forcible passive movement. The child carried the forearm flexed at a right angle, and the supinator longus was felt firmly contracted. Supination and pronation could not be voluntarily performed, but were easily accomplished passively. The hand was carried flexed, and could not be straightened, its range of movement being very limited. Voluntary motion was abolished. The first phalanges of the fingers were extended; the second and terminal, flexed. The first phalanx of the thumb was extended; the terminal, flexed. By passive movement the two distal phalanges of the fingers could be extended, only when the first were flexed. The forearm was wasted only to a degree appreciable by measurement; but the hand showed distinct trophic changes. Thus the dorsum was unnaturally smooth and wasted, and on the palmar aspect, and especially at the tips of the fingers, the skin was smooth and glossy, and on the palm the flexures were very indistinct. The small muscles were atrophied, giving a scooped out palm, and hollows in place of the thenar and hypothenar eminences. Voluntary movement of the fingers was scarcely appreciable, but the slightest degree of flexion and extension could be detected. With the faradic current the muscles of the forearm and hand gave no response; but with the galvanic, good contractions. Sensation in the forearm was normal; but neither touch nor the prick of a pin could be felt at any part of the hand, except over the outside of the first metacarpal bone extending over the thenar eminence for a short distance, in a less distinct degree.

On 13th December, 1895, the musculo-spiral nerve was exposed by an incision three inches in length, crossing the bend of the elbow. The nerve exposed to view was much thickened, and a little below the bend of the elbow, where it divides into radial and posterior interosseous, it was firmly bound down by, and adherent to cicatricial tissue. This nerve exposed, the wound was temporarily closed, and the elbow joint then excised through a single incision behind. The ulnar nerve was next laid bare from the inside of the internal flap. The ulnar was also considerably hypertrophied, and firmly adherent at the level of the joint. It was freed from its adhesions. The median nerve was then exposed by an incision in front. It also was hypertrophied, and firmly adherent to the surrounding cicatricial tissue. It was dissected from its adhesions, but these being very intimate, the portion which seemed to be most involved was excised, that portion measuring about half an inch in length. The ends were then brought into apposition, which was easily effected after the excision of the elbow joint, and sutured by two chromic catgut sutures, passed through the whole thickness of the nerve. The musculo-spiral was then dissected from its adhesions, and as these were very intimate at its point of bifurcation into its two branches, the radial was divided about one quarter of an inch from its origin, and the posterior interosseous about one eighth of an inch from its origin. The terminal portion of the musculo-spiral was then removed about half an inch from its bifurcation, and the two peripheral ends united to the central end of the musculo-spiral with chromic catgut. The wounds were then washed and sutured and drained with catgut. The limb was then fixed in a splint with the forearm semibent.

The dorsum of the hand, the only part exposed, was tested daily for the first sign of returning sensation; but there was no change till the fourth morning after the operation, when there was an indication of improvement, in so far that some sensation, produced by pricking with a pin, was found extending downwards from the wrist, but only for a short distance. There was no further change till the seventh day, when the sensation had travelled down to the level of the midtransverse line on the dorsum of the hand. There was also a point on the inside, which was sensitive On the following day, there was sensation on the inside as far as the head of the metacarpal bone, and also a further extension on the outside. Pricking the skin of the palm with a pin, caused the child to cry with pain. On the ninth day the same conditions obtained, but the child could as a rule locate the region pricked, but occasionally made a mistake. On the eleventh day, there was obscure sensation in the fingers. The improvement continued, and on the seventeenth day the wounds were dressed and found healed, unless at the points where they had been drained. The arm was put on a rectangular splint, and the fingers bandaged out straight. The sensation had now so far improved, that the child could locate the finger pinched, although occasionally she made a mistake. By six weeks, the last occasion upon which the patient was seen, the sense of pain on being pricked with a pin had returned in the little finger, and was quite distinct in the palm, but the other regions of the hand were still insensitive to pain. There was no return of motion, and the electrical reactions remained as before the operation.

Case IV (Plate VIII).

A woman, aged 29 years, sustained a cut with a piece of glass on the right forearm about one inch above the wrist, extending from the front round the inside. The wound was stitched, and healed without trouble, but she soon discovered that she had lost sensation in the little and ring fingers. Shortly afterwards the little and ring fingers and the palm of the hand began to waste, and the skin to assume a smooth glossy appearance. I saw her for the first time on 23rd January, 1896, eighteen months after the accident, when she presented the following condition.

The position of the wound was marked by a linear cicatrix on the right forearm, commencing about the middle line one inch above the wrist, and extending inwards to the ulnar side, curving upwards in its course. The cicatrix was not tender, but, when firmly pressed, a tingling sensation was sent up the arm, and down into the hand. The little and ring fingers were overextended at the metacarpo-phalangeal joints, and semi-flexed at the first and second interphalangeal joints. Both fingers were smooth and glossy, the ring finger showing these characters more so on its inner side. The inner half or three quarters of the palm had a similar shining appearance, and the flexures had almost disappeared. The nail of the little finger was rough, and irregularly grown. The joints of the two affected fingers were stiff, and allowed only a limited range of movement, either voluntary or passive. The two inner fingers could not be brought into contact with the palm, when the hand was firmly closed. There was both on the little finger and inside of the ring, and on the inner half of the palm some slight sensation, but it was of an abnormal character. When touched these parts could be obtusely distinguished, but when pricked with a pin there was no sense of pain. The other parts of the hand were normal.

On 24th January, 1896, the ulnar nerve was laid bare by an incision, extending upwards from the pisiform bone for two and a half inches. The tendon of the flexor carpi ulnaris was found lying ununited, having been divided at the time of the accident along with the nerve. Both the central and peripheral segments of the ulnar nerve were abnormally thick. The proximal segment of the nerve ended in a hard bulb about the size of a small hazel nut, which was adherent to the tissue around. This bulb terminated in a tapering strand of tissue, which, however, had no connection with the distal segment of the nerve. The peripheral segment of the nerve extended upwards behind the central bulb for a short distance, and was very firmly bound down to the deeper tissues by cicatricial bands. There was no bulb upon this, but it presented a conical ending, terminating also in a strand of tissue, which had no connection with the central segment. The bulb was cut off from the central segment, and about one eighth of an inch, including the conical ending, removed from the peripheral segment, and in both cases the exposed sections displayed the appearance of nerve tissue. The nerve was then sutured with chromic catgut, passed through the whole thickness, and, after the tendon of the flexor carpi ulnaris had been repaired, the wound was closed, no drainage being used. The arm was bandaged to a splint with the hand fully flexed.

Three days after the operation, there was distinct sense of touch on the inside of the ring finger, but none, not even the obtuse sensation present before the operation, on the little finger. Five days after the operation, the patient cried out when the inside of the ring finger, or either the back or front of the little finger was pricked with a pin, although her head was covered, and she was unaware of what was being done. On the eighth day the wound was dressed, and found healed, and it was found that the senses of touch and pain over the affected area were good, except at the tip of the little finger, where sensation was not distinct. On the twelfth day the sensation was again tested, and it was found that all parts touched with the point of a pin were correctly localized, except the tip of the little finger. Though felt, sensation was not so distinct as in the normal hand. She cried out when pricked with a pin in any part of the affected area, except the tip of the little finger. The stitches were removed from the cutaneous wound, and on pressure over it the abnormal sensation formerly felt had disappeared, and the flexor carpi ulnaris was felt as a tense cord. The flexion of the hand had been by this time gradually relaxed, and the arm was put on a splint with the hand now extended. Electrical treatment was commenced, and, while the faradic current gave no response, the galvanic current gave contractions on closing, in the small muscles of the little finger, but none could be detected in those of the palm. On the twenty-eighth day, the sensation was again compared in the two hands. The patient then stated that she felt touch on the inside of the palm both back and front and on the inside of the ring finger quite as well as in the corresponding parts of the left hand, but that the sense of touch on the first and second internodes of the little finger, while nearly as distinct, was not quite, while in the terminal phalanx of the little finger, that gentle touches with the point of a pin were felt, but very indistinctly. When pricked with a pin at any point other than the terminal phalanx of the little finger, pain was the result, but in the latter the sensation was only that of touch. By the beginning of the second month, the nutrition of the ulnar distribution of the hand was showing signs of improvement, and sensation was improved in the terminal phalanx of the little finger, pain being felt on pricking with a pin as far as an eighth of an inch from the tip. The thermic sense was tested and found correct. By six weeks from the date of operation, the last occasion upon which she was seen, the atrophy was less though still well marked, and, while the sensation remained almost perfect, there was scarcely any improvement in motion. While she registered 22 kilos. on the dynamometer with the left hand, she could only register 4 kilos. with the right.

Cases of secondary suture are much more valuable for the study of certain questions involved in the regeneration of nerves, than are cases of primary suture. In the former, if the interval of time elapsed from the time of section till the operation undertaken for repair, is sufficient to allow a condition of stable equilibrium of the parts to be attained, the deductions drawn from the results of operation are much less open to dispute. I have shown in the first part of this paper, that theories have been put forward to account for the early return of sensation after nerve suture, without admitting the restoration of conductivity of the nerve, and the question to be decided in the cases just described, is whether the return of function established, is due to a true reunion of the nerve, or if it can be explained in any other way. I would refer especially to the condition of sensation before and after operation. In the first three cases, before operation, it was carefully determined that sensation was totally lost in the regions of the skin supplied by the injured nerves, this loss including not only the sense of pain, but also that of touch. In the fourth case it was also determined, that the sense of pain was absolutely lost in the region supplied by the ulnar nerve, but that there was an obtuse sense of touch present on the little and inside of the ring fingers, sufficient to enable the patient to know, when her finger was touched. I take this to be the mediate sensibility, described by Létiévant (82.) as sensation produced by the impact against the anæsthetic region, being communicated to neighbouring sound papillæ, and thus conveyed along other nerves, without any direct nerve communication existing between the part touched, and the nerve conveying the impulse. Thus the impulse produced by touch might in this case have been conducted along the median or radial nerves, and learned by experience by the patient to be, from its obscure character, referred to the anæsthetic area. The absence of the sense of pain pointed to the conclusion, that the ulnar nerve was not conducting, a conclusion which was justified at the operation, as the nerve was found completely divided, and the ends lying apart. Leaving out of account the case in which the nerves were compressed at the seat of fracture, these observations were made at three, six, and eighteen months respectively, from the time of injury, and after the operation, the sense of pain made its appearance in one at the end of two days, in one at the end of three days, and in one at the end of five days. I have already quoted some of the published cases with similar results, and shown that none of the theories, which have been advanced to account for early return of sensation by channels other than that of the injured nerve, are applicable to such as these. The finer anastomoses described by Arloing and Tripier (70.), or coarser anastomoses cannot have existed in these cases, as the sense of pain was totally lost; and the delay between the division of the nerve and the operation, without any return of sensation, shows that no replacement, either by outgrowth from neighbouring nerves as supported by Tillmanns (123.), or by development of fine collateral anastomoses as held by Remak (87.), could have taken place. The speedy return of sensation after the operation, therefore, leaves only the conclusion that the return was the result of restoration of conductivity in the injured nerve. In making the tests for returning sensation, the sense of pain was always taken by means of pricking the skin with a pin, in order to avoid the possibility of mistaking mediate for immediate sensibility; for by mediate sensibility only touch is appreciated, and pricking the skin with a pin if felt, would only be as tactile sensation.

From the time of the first appearance of the sense of pain, sensation gradually improved in the further course of the cases; but the cases showed differences in progress. At first localization of sensation was imperfect, but this very soon was developed, and in about a month from the time of operation in two of the cases, the gentlest touches were distinctly felt, and correctly localized. In one of the cases the tip of the forefinger, and in another the tip of the little finger were particularly long in developing sensation. In the case in which the nerves were interrupted at the seat of fracture, the return of sensation was less satisfactory, and it was not till the eighth day, that the sense of pain appeared in the palm, and not till six weeks, that it commenced to return in the fingers. This delay must be explained by the different nature of the lesion in this case from that in the other cases. In the latter the injury to the nerve was merely division, while in the former an indefinite length of nerve was injured by the pressure of cicatricial tissue; and although portions were removed which seemed to be most involved, doubtless there were portions at a lower level left, which were also much damaged by the pressure. The return of sensation in the ulnar distribution in the first case, is particularly remarkable; for in that case, the divided ends of the ulnar nerve could not be brought together, nearer than a quarter of an inch; and, yet, in the little finger the sense of pain was developed in three days. It must, therefore, either be supposed that the interval between the nerve ends was bridged over in that time by a substance capable of conducting, or that by anastomotic fibres the impulses were conducted along the median nerve, in which the ends had been brought into apposition; but from the speed with which sensation in the little finger became perfected, it is more likely that the first view is correct.

In no case did improvement occur in the muscles, until a comparatively late period, and as far as I was able to trace the cases, this function only approached a perfect recovery in one case (Case II), and even in that case at the end of a year, it was still improving. This delay in the return of motion, is an almost generally observed occurrence, and some authors explaining away the return of sensation, take only return of motion as a proof of the restoration of the conductivity of the nerve. But the delay in the return of the motor function is easily intelligible, when it is remembered that for the recovery of motion not only the nerve, but also the muscle has to recover; while for sensation only the recovery of the nerve with its end organs is necessary. The injury to the muscle is not only the result of its long inactivity, but also of its long separation from its trophic centres. Thus it is that in all the cases, even the third case, where the separation from the centres must have been less than two months, the muscles affected showed great atrophy, and tested electrically gave the reaction of degeneration. Supposing, then, their nerve supply to be restored at the time of the first appearance of sensation, the muscles only then would begin to recover, and, in their weakened condition, their recovery must necessarily be a very slow process; and, indeed, it is intelligible that in some cases the muscles would be incapable of repair from their complete degeneration. The gradual improvement in the first case, was demonstrated by the return of faradic irritability in the small muscles of the thumb, one and a half months after the operation. The return of motion is also hindered by stiffness in the joints; for, in one of the cases, although at the end of a year all atrophy had disappeared, and opposition of the thumb to the tip of the little finger, and abduction of the thumb were easily performed, and although the strength of grip as tested by the hand dynamometer, was almost as good as that of the sound hand, yet the stiffness of the terminal joints of the index and middle fingers interfered with the strength of grip for smaller objects, as it was impossible to bring the tips of these fingers into the centre of the palm. (Plates IV and V.)

The operation in none of the cases gave rise to any untoward symptom. Temperature remained normal throughout, and the wounds healed by first intention. In the second case, however, after the wound had apparently healed by first intention, a small abscess formed, and pointed in the line of incision. On opening it the sutures, which had been employed for the nerve, came away, and the wound then speedily healed.

The condition of the nerves found on exposing for suture, was not the same in every case. In every case the nerves appeared thickened as far up and down as they were exposed, and this was not only exhibited in the central segment, but also in the peripheral. The usual description of the peripheral segment, which has been some time separated from the central, is that it is found atrophied, but I did not find this in any case. On the contrary, when the nerve had been sutured, it appeared as a cord of uniform thickness above and below the seat of suture. The divided ends of the nerves were found in one of two conditions. In two of the nerves, they were united by a bulky cicatricial mass, while in two, they were lying apart without any apparent connection one with the other. Where the nerve ends were united, this union was evidently not such as to enable function to be carried on. Where the ends were lying apart, the central end in both cases presented a bulb of hard consistence, in one case ending in a tapering filament; while the peripheral end presented in the one case a small hard bulb, and in the other a conical ending. What may have had something to do with the different character of the two peripheral ends, is the fact that the end with the bulb was lying free in loose connective tissue, while the end with the cone was lying firmly bound down to the underlying structures by means of cicatricial bands. The prevailing opinion is that it is useless to do more than raw the peripheral end before suturing, but I always cut off the terminal portions, and the sections exposed always showed an appearance resembling the section of a nerve.

Microscopical Examination.

Methods. In every case the portions removed were immediately put into Müller's fluid, in which they remained for several weeks, the fluid being changed at intervals. After dehydration, they were then imbedded in paraffin, and both longitudinal and transverse sections prepared with the Cambridge microtome, the sections being cut as thin as possible. The sections were then fixed by the albumen method on slides in series, and stained by various methods. The methods which I found to give the most useful results, were the first method of Weigert* and the anilin-blue method of Stroebe (156). I found it useful after staining by Weigert's method, to stain the preparation first with safranin, and then with eosin, as by that addition the distribution

* vide. Lee. The Microtomist's Vade-mecum. Lond. 1893. 3rd ed., p. 362

of the nuclei, and of the connective tissue was very clearly demonstrated.

The following table shows the portions examined.

Part examined.	Nerve	Case	Time between injury and excision.
Central bulbous end.	Ulnar	I	6½ months.
do.	do.	IV	18 do.
Peripheral bulbous end.	do.	I	6½ do.
Peripheral conical end.	do.	IV	18 do.
Cicatricial intermediary segment.	Median	I	6½ do.
do	do	II	3 do.
Portion compressed at seat of fracture.	do	III	Uncertain: Not less than four weeks.
do	Musculo-spiral with Radial and Interosseous	III	

Central ends. The bulbs from the central segments were both very dense with smooth surfaces. One lay surrounded by loose connective tissue, while the other was adherent at its lower end to surrounding cicatricial tissue. The latter had a terminal filament, but with that exception their appearance was similar. The following are the microscopical characters of that from the ulnar of case I.

Under a low power (Plate IX), a longitudinal section shows the nerve entering the bulb at the side. The individual fasciculi bend round in entering the bulb, and when they have entered, the fibres diverge, and spread in different directions throughout the bulb, the fasciculi presenting thus at their entrance a fan shape. The bulb itself has a clearly demarcated outline of connective tissue, but its interior presents a heterogeneous aspect. In a common ground of connective tissue, there is everywhere thickly scattered small bundles of nerve elements. These bundles are cut in all directions, some transversely, appearing as small round points, others longitudinally, appearing as lines which frequently bifurcate, and others, in all degrees of obliquity. Here and there multitudes of transversely cut bundles are grouped together in islets, surrounded by longitudinally cut bundles

Under a high power (Plates XI, XIII, and XV.), the upper part of the entering fasciculi show chiefly normal nerve fibres, but the lower part, while showing occasionally a normal nerve fibre, is made up of a mass of delicate bands. While the old fibres measure in diameter about 9μ ($\frac{1}{2800}$ inch.), the bands measure only about 3μ ($\frac{1}{8400}$ inch.) in diameter. They have attached to their sides numerous nuclei, the length of which is from five to eight times their breadth, the more elongated measuring 13 μ ($\frac{1}{1900}$ inch.) in length, and 1·6 μ ($\frac{1}{16000}$ inch.) in breadth. These bands have a granular appearance, and there is little doubt of their being young nerve fibres, seeing that in the centre of many, a delicate thread, the axis-cylinder, can be clearly distinguished. In many, also, Weigert's method brings out a delicate myeline sheath, appearing as closely set bluish black granules. In the fasciculi which enter the bulb, these new formed fibres lie in bundles, separated by a few connective tissue fibres, running parallel with the nerve fibres. In the region of transition between the old fibres and the new (Plate XV), an actual connection between the axis-cylinders of the old and those of the new, cannot be traced. What, however, is clear is that each bundle of new fibres corresponds to a single old fibre, and in many cases, the old fibre can be seen tapering off, its place being taken by the new fibres, the number of new fibres becoming greater as the old fibre diminishes, until finally only new fibres remain. In tracing further downwards the groups of new fibres, the number contained in a single bundle increases, and, while the bundle is thereby increased in diameter, the fibres themselves retain a fairly uniform breadth.

Passing into the bulb, there are here no old fibres to be found, but the whole structure is made up of bundles of new fibres, cut in every direction, and surrounded by a small amount of fibrous tissue. The bundles cut transversely, are small in diameter (Plates XI and XIII), yet the larger contain an enormous number of young nerve fibres. These fibres appear as clearly defined circles, containing each in its centre a distinct axis-cylinder. The more prominent have a diameter of 3μ ($\frac{1}{8400}$ inch.), but there are some which have not more than half that diameter. Many have attached to their sides, a nucleus which here has a circular outline, but which when compared with those in a longitudinally cut bundle, is seen to be a section of a spindle-shaped nucleus. The whole bundle is surrounded by a layer of connective tissue, but there is no sheath proper. The fibres which show longitudinally, present the same characters as the new fibres in the entering nerve, already described.

Transverse sections of the upper part of the entering nerve in the central bulb of Case IV, show that at this point the nerve has retained its normal arrangement of fasciculi. While some of these fasciculi have retained at this level their normal fibres, others have no old fibres, but instead, groups of young fibres. (Plate XVI). These young fibres present characters identical with those of the fibres in the bulb already described, but as a rule only from three or four to a dozen are grouped together in a single bundle. These bundles resemble very closely both in number and in disposition, the arrangement of the single old fibres in neighbouring fasciculi in which the latter have been retained. Around these fasciculi the perineurium and epineurium present normal characters, and the endoneurium appears also to be normal.

The examination of the filament in which the bulb terminated, was made by serial transverse sections. It is composed almost entirely of connective tissue, but at its upper end, there are about twenty or thirty small bundles of new nerve fibres. Proportionately as the sections are taken from lower levels, the number of nerve fibres diminishes, and the last section examined, still some distance from the termination of the filament, contains only three small bundles, each containing three or four young nerve fibres.

Peripheral ends. The bulbous end, removed from the peripheral segment of the ulnar in Case I, was about half the size of that removed from the central, and had also a firm consistence

Under a low power (Plate X), it presents a groundwork of connective tissue, in which lies tissue, stained bluish black with Weigert's method. This tissue runs in bundles, longitudinally from the point at which the bulb was removed, towards the free end. About the middle of the bulb, the more regular longitudinal course of these dark stained bundles ceases, and the remainder of the section is occupied by the same tissue, cut transversely and in various degrees of obliquity, showing many circular bundles, isolated or in groups, with a few bundles running longitudinally for a short distance among them.

Examined with a high power, the sections show no old nerve fibres, but the tissue stained by Weigert's method, is identical in characters with the new nerve tissue seen in the central bulb. In the distal half of the bulb, the fibres run chiefly longitudinally, and are grouped into bundles, each of which contains many nerve fibres. These young fibres have the same characters as those in the central bulb. Thus they have the same average diameter, have attached to their sides at very short intervals elongated nuclei, and have in many cases a delicate myeline sheath. In many a distinct axis-cylinder is visible, occupying the centre of the fibre. The bundles are separated by fibrous tissue in greater or smaller amount, and in this tissue, are a number of round cells with granular contents. A few bundles appear, cut transversely, beside those cut longitudinally. In the proximal half of the bulb, it is rare to get the fibres running for any great distance in one plane. Thus the majority appear cut transversely or obliquely. The connective tissue here is in larger quantity, than at the attached end of the bulb. The bundles of nerve fibres cut transversely, are of different size, but, irrespectively of that difference, the contents are identical. They contain (Plates XII and XIV) from a few up to twenty or thirty closely aggregated young nerve fibres. The larger of these measure in diameter 3µ ($\frac{1}{8400}$ inch.), have a well defined circular outline, and contain each in its centre a distinct point, the axis-cylinder. There are also many much smaller fibres with similar characters. The bundles also contain the sections of nuclei, the larger of which are about one half the diameter of the larger fibres. Around the bundles one or two layers of connective tissue are arranged concentrically, but there is no definite sheath.

The conical portion removed from the periferal segment in Case IV, also contains no old nerve fibres. It has a very dense structure, the nerve elements and connective tissue being very closely aggregated together. A few transverse sections removed from the base of the cone, show the majority of the new fibres in bundles cut transversely (Plate XVII), but even at that level a few are cut longitudinally and obliquely. Similarly in longitudinal sections of the cone, there is no part in which the bundles run exclusively in one direction. Towards the apex of the cone the number of fibres diminishes, and the section appears entirely composed, ultimately, of connective tissue. The characters of the fibres here are identical with those of the fibres already described, but a few show more distinctly than those either in the central or peripheral bulbs of Case I, the formation of the myeline sheath. In some of the fibres, it has taken on the stain so deeply, that the contents of the fibre are quite hidden, and appears as a uniform granular coat.

The cone terminated in a filament about half an inch in length, and this was examined for nerve fibres by serial transverse sections, but none were found. The core of the filament is occupied by a bloodvessel, and the remainder is simply connective tissue.

Intercalary cicatricial segments. The cicatricial mass which united the two ends of the median in Case I, measured half an inch in length, and three eighths of an inch in breadth. It had a rough and somewhat irregular surface, and firm consistence. It was thicker in the middle, and narrowed to the thickness of the nerve at either end.

Transverse sections from its proximal end (Plate XVIII), show a network of dense fibrous tissue, containing in its meshes bundles of nerve elements. In some parts the connective tissue fibres run longitudinally, appearing as points in section, but in others they run transversely, being there displayed in a large part of their course in the section. The bundles of nerve elements are uniformly distributed throughout the section, but they are small, the larger measuring only 30μ (1/840 inch) in diameter, and are isolated from each other by a considerable breadth of dense fibrous tissue. Some are very small, containing only two or three fibres, while the larger contain as many as twenty. All the fibres exposed are small new fibres, no old fibres being present. These fibres agree in characters with those already described. They have a very sharply defined outline, the axis-cylinder is very distinct, and there are many nuclei lying between them, and attached to their sides. Many of these fibres are larger than any met with in the other cases, some measuring 4μ (1/6250 inch) in diameter.

The peripheral end of the mass presents a less regular aspect. In some parts (Plate XIX), there are dense masses of fibrous tissue, and only isolated bundles of nerve elements, grouped together, while in other parts (Plate XX) the distribution of the nerve elements is very uniform. These uniformly distributed bundles are still smaller than the bundles in the proximal end, the largest measuring 17μ ($\frac{1}{1500}$ inch.) in diameter, but the majority much smaller. The larger contain eight or ten young fibres, and the smaller from two to three or four. In addition to these, there are many isolated fibres. The young fibres are the same in structure, as those in the opposite end of the mass. The bundles do not all appear in transverse section, but a few appear running longitudinally in the section, and, therefore, transversely in the mass, and a few obliquely cut. In these the spindle-shaped nuclei, attached to the sides of the fibres, are displayed. Also in many such fibres the axis-cylinders are shown as delicate threads. (Plate XIX.)

The characters of this mass, which have been described from transverse sections from its two opposite ends, are shown by longitudinal sections to be maintained throughout the whole mass. The arrangement of the bundles is very irregular. In the same longitudinal section are to be seen islets of transversely cut bundles (Plate XXI), and coursing around them, bundles cut longitudinally and obliquely. Some of the longitudinally cut bundles contain fibres, which show very well the developing myeline sheath, not however sufficiently dense to hide the delicate axis-cylinder. (Plate XXII)

The intercalary mass from the median of Case II, agrees in characters with that just described so closely, that a separate description is unnecessary.

Portions compressed at seat of fracture. The portion excised from the median, and that from the musculo-spiral with its two branches, are examples of nerves, which have been under compression for several weeks.

The portion excised from the median, measured in length only about half an inch, yet transverse sections from the proximal and distal ends, show very different structures. The transverse section of the proximal end (Plates XXIII and XXV) is practically that of a normal nerve, showing throughout a normal subdivision into fasciculi, surrounded each by a normal perineurium, and each containing normal myeline fibres, the majority of which measure about 8μ ($\frac{1}{3125}$ inch) in diameter. The section agrees in every particular with transverse sections of normal human nerves, which were treated by the same methods for comparison.

The transverse section of the distal end shows a normal subdivision into fasciculi, and, under a very low power (Plate XXIV), looks like the section of a normal nerve, with the exception that, treated by Weigert's method, the fasciculi are not stained so deeply. With a high power, however, (Plate XXVI) the difference from the normal nerve is very decided; for the fasciculi contain no old myeline fibres, but in their place, groups of young fibres. The perineurium surrounding each of the fasciculi has a normal appearance, but the endoneurial tissue has if anything, a stronger development than normally. The groups of young fibres are small, the majority measuring about 8μ ($\frac{1}{3125}$ inch) in diameter, with here and there a few larger examples. As a rule they contain only three or four young nerve fibres, each presenting a sharp circular outline, and containing an axis-cylinder in its centre, together with one or two nuclei, either lying between the young fibres or at the circumference of the small bundle. Most of the bundles are surrounded by a delicate membrane. All the bundles shown in the section, are transversely cut. The epineurium is normal, and no young fibres are found between the layers of the perineurium.

The portion removed from the musculo-spiral nerve and its two branches, included the terminal half inch of the former, with a quarter of an inch of the radial, and an eighth of an inch of the posterior interosseous. The transverse section of the proximal end of the musculo-spiral is normal; while those of the distal ends of the radial and posterior interosseous present no old nerve fibres, but instead, groups of young fibres, arranged as in the distal end of the portion of the median just described. In the transverse sections which have passed through the region of transition from the old fibres to the new, some of the fasciculi show an arrangement of old myeline fibres which is that of a normal nerve, but many of the myeline fibres have an abnormal character. In the simplest of these, the axis-cylinder is greatly hypertrophied, and the whole fibre is enlarged (Plate XXVII). In others, between the sheath of Schwann and the myeline sheath, is a large nucleus, presenting a circular outline. In another, in addition to the large nucleus, and lying alongside of it, are one or two very distinct young nerve fibres with clearly defined circular outlines, and delicate axis-cylinders; while the myeline sheath of the old fibre is indented by the new-formed structures, and the old sheath of Schwann is slightly distended outwards. (Plate XXVIII). The old fibre, however, has still its characters preserved. Most such old fibres measure about 12μ ($\frac{1}{2100}$ inch.) in diameter, while the new fibres intercalated between the sheath of Schwann and the myeline sheath, measure 3μ ($\frac{1}{8400}$ inch.) in diameter, and the nucleus has a diameter approximately the same. Other old fibres in the same section present three, four, and up to a dozen newly formed fibres lying in the same position, and the number of nuclei present is proportionately increased to two, three or more. Just as the old fibres present a greater number of young fibres, so the old myeline sheath and axis-cylinder appear crushed to the one side and diminished (Plates XXVIII and XXIX). In some in which the old sheaths of Schwann contain about a dozen new fibres, traces of the old axis-cylinder and myeline sheath can still be seen at one side of the group; while in other cases, no trace of the old myeline sheath and axis-cylinder can be found, and there is merely a group of young fibres with nuclei, surrounded by the old sheath of Schwann. Those old fibres which still contain the myeline sheath and axis cylinder, and yet have young fibres between the myeline sheath and sheath of Schwann, show the latter sheath distended in proportion to the number of young fibres present. Also, where the myeline sheath and axis-cylinder of the old fibres have disappeared, many show the old sheath of Schwann, surrounding the group of young fibres; but in some where the number of young fibres in a bundle is great, the old sheath of Schwann is very difficult to trace.

A longitudinal section made through the same region, shows the old myeline fibres terminating, and giving place to the young fibres (Plate XXX); and the sheath, enclosing the bundle of young fibres, can often be traced into continuity with the old sheath of Schwann. The more common condition traced from the old fibre above down into the bundle of young fibres, is as follows. The old fibre gradually increases in diameter, and presents finally, what approaches a bulbous condition. In its interior the axis-cylinder is swollen, and presents in many cases a bulb. Beyond this the old myeline sheath and axis-cylinder contract greatly, and terminate almost immediately. The sheath of Schwann is continued beyond the bulbous myeline fibre, as the sheath surrounding the bundle of young fibres. Often, before the termination of the old fibre is reached, isolated young fibres can be seen, running between the sheath of Schwann and the myeline sheath. These pass downwards, until they are lost in the bundle of young fibres beyond the old. The nuclei seen in transverse sections as circular, are here shown spindle-shaped.

Conclusions from the microscopical examination.

Degeneration. The length of time which has elapsed from the time of injury till the examination of the nerve in these cases, precludes the study of the earlier stages of degeneration, but allows certain deductions concerning the later stages and final result of the process.

The sheath of Schwann, notwithstanding

the lapse of several weeks from the commencement of compression, still remains in the portions of nerve from Case III. (Plate XXVI). It can be traced downwards from the old fibre into the region of the new fibres, where for a time it is retained. (Plate XXX). But as the new fibres increase in numbers, the old sheath is gradually distended, and ultimately becomes unrecognisable, probably becoming part of the endoneurial connective tissue. This then accords with the view expressed in the recent papers by Büngner (150.), Howell and Huber (154.), Stroebe (156.), and Notthafft (157.) that the sheath of Schwann is retained for a time after degeneration of the other parts of the fibre, but that it is destroyed during the regenerative process.

Where the old sheath of Schwann is still retained, it contains nothing which could be taken for the old axis-cylinder. The latter, traced into the region of compression, is seen terminating often in bulbous ends, and below that, the contents of the old sheath are only new formed elements. (Plates XV. and XXX) In other cases, the gradual disappearance of the old axis-cylinder can be seen in transverse sections through the point of transition from old to new fibres (Plates XV and XXX). In the portions of nerve removed from periferal segments, there are no old fibres to be seen; and no structures which could be taken for old axis-cylinders. My results are therefore, not in accord with the view taken by Schiff (31.) Philipeaux and Vulpian (39.) Wolberg (127.) and others, that both the old sheath of Schwann and the old axis-cylinder are retained in the whole peripheral segment. Ranvier (102.) also, while he finds that the axis-cylinder is destroyed in the peripheral segment, holds that it is retained in the central, unless exceptionally, and that the degenerative process affects only the extremely small portion of the central segment measured by one or two of the nodes now called by his name. But in the central bulbs examined, there are portions of the old nerve about a quarter of an inch, attached to the side of the bulb, and it is only at the extreme upper part of this that old fibres are present, while the remainder is entirely occupied by new fibres, among which no trace of the old axis-cylinders is visible.

The view taken by Krause (136.) that

the sensory fibres from the touch corpuscles of Wagner and Meissner, having their nutritive centres there, undergo degeneration in the central segment, while they remain sound in the peripheral segment, has been taken as an explanation of the conflicting results of other authors. Krause found that transverse sections of the central segment showed about one half of the fibres degenerated, while he merely assumed that in the peripheral segment there were a corresponding proportion of the fibres which remained sound, his assumption being based on analogy with the condition found in rabbits. But in the transverse sections made from the proximal ends of the portions from the median and musculo-spiral nerves of Case III, the appearances presented are those of a normal nerve (Plate XXV): in none of the fasciculi are any new fibres found, and there has, therefore, been no degeneration. Also in portions removed from peripheral segments, no old fibres are present. I cannot, therefore, agree with Krause that there is an ascending degeneration in the central segment; for the proportion of fibres indicated by him as becoming degenerated in the central segment, is so great that there would be no difficulty in seeing them if present, or the resulting regeneration in any case. This is also the opinion expressed by Gottsacker (145.) from examination of stump neuromata. From the account given by S. Meyer (100, 108, 125), Hammer (159.), and Teuscher (149.), it would appear that in any nerve there are always to be found degenerated fibres; but that these are present only very sparingly, and are due to a normal process of degeneration. Krause's results were obtained from the examination of nerves in limbs amputated for gangrene. Several of these were senile or diabetic gangrene, and it is, therefore, possible that in his cases the degeneration of the nerve was primary to the gangrene. This is more likely, if we are to regard with S. Meyer, the nerve fibres not as perennial structures, but as undergoing a normal process of degeneration and regeneration, and this view is supported by the work of Korybutt-Daszkiewicz (105), who found an active formation of nerve fibres in the nerves of the frog, on placing the frogs in favourable surroundings, after a period of starvation. In any case, if an ascending degeneration were caused by interruption of the course of a nerve, there would have been some evidence of that in the transverse sections of the proximal ends of the median and musculo-spiral portions from Case III.

<u>Regeneration of nerve fibres in the peripheral segment, while still separated from the central segment.</u> The portions of nerves examined, show very clearly, not only that in regeneration the young fibres are produced both in the central and in the peripheral segment, but, also, that reunion of the ends is not an essential to the production of young fibres in the peripheral segment. This independent origin of new fibres in the peripheral segment, without previous reunion with the central end, first observed and described by Philipeaux and Vulpian (38, 39.), has been opposed by almost all who have since made a study of regeneration of nerves, and their opinion was also greatly weakened by the fact that Vulpian (77, 86) himself withdrew from his former position. Mitchell (80.), and recently Bowlby (146.) have found in the examination of portions

removed from the peripheral segments of un-united divided nerves, that many newly formed nerve fibres are there present. The opponents of this view give various explanations of the results of these observers. Some hold that Philipeaux and Vulpian mistook products of degeneration for young fibres; Schiff (41.) and Ambrosoli (43) that their results were only to be got in very young animals; while Ranvier (102), again, thinks that they did observe the peripheral segment regenerated, but that they had failed to observe certain strands of tissue between the central and peripheral ends, through which the peripheral segment had been regenerated. He supports this allegation by an observation of his own, where a central segment lying separate from its peripheral, was connected to it by a membrane having the appearance of connective tissue, but which contained nerve fibres, as shown by the tint which it took on being subjected to the action of osmic acid. Howell and Huber (154). in opposing the results of Bowlby, hold that the young fibres which he observed, were simply sections of nuclei, and that the point in their interior, taken for the axis-cylinder, was nothing more than the nucleolus, and state that this explanation is more likely, since Bowlby figures no nuclei among the bundles of fibres. It is true that in Bowlby's figures there are no nuclei shown among the young fibres, and he believes that the axis-cylinders are formed by the nuclei. But in my preparations there can be no doubt of the structures in question being young nerve fibres; for the axis-cylinder shown in transverse section as a point, is clearly visible in many fibres seen longitudinally, as a delicate thread. Also in the bundles which are cut transversely, nuclei are always present, lying between the fibres, and in many cases distinctly apposed to the fibres; and in fibres seen longitudinally these nuclei are spindle-shaped, and distinctly attached to the sides of the fibres. The difference between the axis-cylinders and the nuclei of a bundle is well shown in some of the preparations, which were stained by the method of Stroebe; for the former have taken on the aniline blue, while the latter have taken the red colour of the safranin. But that they are really nerve fibres, does not rest alone on the axis-cylinder being demonstrated, for they also in many cases show a commencing myeline sheath. In order to find, if they could possibly have been communicated to the peripheral segment from the central end of the nerve, through fine bands of tissue connecting the ends as suggested by Ranvier, I made a careful search for such. In one of the cases such were present, in the form of fine filaments, one attached to the central end, and one to the peripheral, but without any connection one with the other. In that attached to the peripheral, there were no nerve elements present, while in that taken from the central end, the upper portion contained only a few isolated bundles of young nerve fibres, which gradually diminished in numbers as the sections were taken further off from the bulb, until in the last section taken, still some distance from the termination of the filament, only three small bundles remained. I found, therefore, no means of communication between the ends, and must conclude that the young fibres observed in the peripheral segment have an independent origin there.

Vanlair (122) found in the sciatic nerve of a dog, that four months after resection of a portion, there was reunion of the ends by a cicatricial segment, but no functional return. The cicatricial segment, he found regenerated, but the peripheral segment contained only fibres which he regarded as end products of degeneration, and called "atrophic degeneration". His description of these fibres agrees with the appearance presented by newly formed fibres, and I think it probable that they were such, and not the products of degeneration.

The origin of the young fibres. The arrangement, wherever they are found, of the new fibres in bundles suggests that the fibres composing each bundle have had a common origin. As a rule the number contained in a single bundle is great. The part of the nerve in which they originate, can be seen, when sections from the central segment close to the termination of the old fibres are examined; for, while the young fibres are there seen still in bundles, these bundles are small, and contain few young fibres. The diameter of these small groups of fibres is approximately the same as that of a single old fibre, and the sheath of Schwann can be traced down in longitudinal sections, from the old fibre into the region of the new, where it is seen surrounding the small bundle of new fibres. (Plates XXVI and XXX).

It is clear from this, that these young fibres originate within the sheath of Schwann. On tracing them downwards in longitudinal sections, they are found to increase in numbers and distend the sheath of Schwann, which ultimately becomes unrecognisable. It is, thus, probable that the young fibres of each of the bundles which appear in the central bulb and in the end of the peripheral segment, represent in most cases fibres which have had a common origin from within one old sheath of Schwann.

The epineurium and perineurium appear normal in the portion of nerve immediately proximal to the central bulb, and in the portions removed from the seat of compression (Plates XVI and XXVI). There is, therefore, nothing to indicate an origin of nerve fibres from the cells of the perineurium, as described by Hjelt (44.) Wolberg (127.) and Hanken (143.). Also the view of Vanlair (122.) that the new fibres proceed into the perineurium, and out into the epineurium, forming a zone round the fasciculus has nothing to support it in my preparations.

If, then, the new fibres originate within the old sheath of Schwann, they must be formed either by growth from the old fibre above as described by Ranvier (81, 102) and others; or from the remains of the old fibre, as held by many; or from the protoplasm and nuclei of the sheath of Schwann, as held by Büngner (150) and others. The manner in which the old fibre ceases abruptly, and gives place to many young fibres which occupy the continuation of its sheath of Schwann, may suggest an origin such as described by Ranvier and others; but the presence of undoubted young nerve fibres in the peripheral segment, while it has no connection with the central segment, is incompatible with this view. The young fibres also cannot originate from the remains of the old, as in the region of transition from the old to the new both old fibres and young are seen enclosed within a common sheath of Schwann (Plates XXVII, XXVIII, and XXIX.) Thus the only source left from which to derive the young fibres within the old sheath of Schwann, is the nucleus and protoplasm of the interannular segment. This conclusion is strengthened by the examination of transverse sections, passing through the point of transition from the old fibres to the new; for there, the old fibre can be seen with one or more young fibres lying beside the nucleus, and between the sheath of Schwann and the myeline sheath (Plates XXVII to XXIX) The enormous number of spindle-shaped nuclei among the nerve fibres, indicates that these structures have originated by proliferation from the nuclei of the sheath of Schwann, but in my preparations the proliferative stage had evidently come to a conclusion, as no indications of karyomitosis were present.

My results are, therefore, in accord with the opinion expressed in Büngner's recent paper, that the nuclei and protoplasm of the interannular segments must be viewed as neuroblasts, their function being to produce new nerve fibres. And taking into account the observations of S. Meyer (100, 108, 125), it would appear that the exercise of their function is not reserved for accidents such as nerve section, but occurs normally, the fibres undergoing a normal degeneration and regeneration. The bundles of young fibres were seen by Howell and Huber (154.) in the peripheral end of nerves which had not united, but having failed to stain the axis-cylinder they call them "embryonic fibres", and find that they receive an axis-cylinder only by growth of the latter from that of the old fibres in the central end. That these fibres observed by Howell and Huber were really nerve fibres, is shown by the fact that when the peripheral segment, containing only such, was mechanically irritated, a low degree of irritability and conductivity was found.

Characters of the young fibres. The young fibres appear with a central axis-cylinder with a protoplasmic surrounding zone, having a well defined outline, and with spindle-shaped nuclei attached at short intervals to their sides. It is evident, therefore, that the nuclei do not form the axis-cylinder as described by Bowlby (146.), but that in the formation of the fibre, only the central portion becomes developed into the axis-cylinder. In many fibres both in the central and peripheral ends, the protoplasmic zone contains a granular deposit which takes on the characteristic tint of myeline by treatment by Weigert's method (Plate XXII). It is, therefore, clear that the myeline sheath is deposited in the protoplasm gradually and uniformly. In transverse section the young fibres correspond in appearance and diameter (3μ) with the "fibres à gaîne vitreuse" of Vanlair (122), and according to him the "gaîne vitreuse" is a provisional covering of the axis-cylinder, derived from the connective tissue around, which becomes thinner as the normal sheaths of the axis-cylinder develop, and finally becomes the fibrillar sheath. I think it more probable that the zone surrounding the axis-cylinder, is the protoplasmic residue not used up in the formation of that structure, and that after the myeline sheath becomes deposited within it, it remains with the nucleus as the protoplasm of the interannular segment.

Independently of the time which has elapsed from the injury till the excision of the portions of nerve examined, the stage of development of the young fibres is the same, with the exception that some show more distinctly than others the commencing myeline sheath; and this similarity occurs both in the central and peripheral ends. As this time varied from a few weeks to eighteen months, the development presented by the fibres must be regarded as a resting stage. It is probable that the further steps in development to the adult fibre depend on a restoration of continuity of the nerve, and that, such as would allow the transmission of impulses through the young fibres. Also the observation of Philipeaux and Vulpian (39.) that regeneration is more rapid when union is effected may be explained on the view, that reunion is necessary to the further development of the fibres. That these young fibres are capable of transmitting impulses, I take the observations of Howell and Huber as proving; and this explains also why after the operation of suture, so rapid a return of sensation in the parts previously anæsthetic occurs.

With regard to the formation of the new sheath of Schwann, it might be viewed as a metamorphosed outer layer of the young fibre, but this is unlikely from the behaviour of the old sheath. For since that structure does not degenerate along with the rest of the fibre, and is only finally destroyed or displaced by the mechanical condition that it is no longer able to contain the developing fibres, it does not act as part of the fibre. It is more probable that it is an addition to the fibre from the surrounding connective tissue.

On comparing the transverse section of a nerve made through a part which contains the old fibres, with one made further down in the region containing new fibres, the increase in numbers of the new fibres as compared with the old is very striking. It is seen that the number of groups of new fibres is approximately equal to the number of old fibres, and as each group contains at a high level three or four, and at a lower, many more, the numerical increase may be roughly estimated (Plates XXV and XXVI). It is hardly likely that all such fibres are developed to the stage of mature fibres. It may be that when reunion is established, only the normal number of fibres develop further, while the others perish or remain undeveloped; but this is a subject upon which there is as yet no evidence.

<u>Cicatricial intercalary segments.</u> The nature of the cicatricial mass, uniting two ends of a nerve by a bond which does not allow reestablishment of function, is illustrated by two of the cases. In these, although the mass has the appearance of cicatricial connective tissue, yet the microscopical examination shows that from end to end the mass contains a rich supply

of young nerve fibres. But at the same time, these young fibres are separated by much dense connective tissue, which in some places is massed together to the exclusion of young nerve fibres. (Plates XVIII to XXII). This mass has evidently been supplied with nerve fibres by immigration into it of neuroblasts either from the central end or from both. I think from both ends, from the fact that both central and peripheral ends of nerves, remaining entirely separated, show at their ends a mass of connective tissue containing nerve fibres. The latter do not run in parallel lines, as they do when met in a piece of old nerve, but are convoluted, showing that they have been developed in the irregular spaces of the connective tissue. But if a cicatricial mass connecting the two ends of a divided nerve is thus supplied with nerve fibres from the central and peripheral ends, there must be some cause preventing the transmission of impulses. The explanation which seems to me most probable, is that if there has been much inflammation in the parts, the amount of cicatricial tissue in the mass is so great that by the time the mass is bridged over by nerve fibres, the contraction of the cicatricial tissue has become so great, that the nerve fibres are prevented from transmitting impulses or developing further, in a way exactly analogous to that which occurs, when a nerve is involved in the callus of a fracture.

Briefly my conclusions are as follows:-

1st. That ununited divided nerves sutured long after division, can reunite and transmit impulses in a few days.

2nd. That after division or interruption of a nerve, there is no ascending degeneration as described by Krause.

3rd. That the old axis-cylinder is destroyed in the peripheral segment, and in the ultimate portion of the central segment.

4th. That new fibres originate in the peripheral segment as well as in the central end.

5th. That the formation of new fibres in the peripheral segment occurs, although there is no connection with the central end, but that maturation of the fibre is not completed, while separation of the ends lasts.

6th That the new fibres originate from cells within the sheath of Schwann.

7th That in the development of the young fibres, the central portion of the primitive protoplasmic band forms an axis-cylinder, and the myeline sheath is deposited in the surrounding protoplasmic zone, which latter remains along with the nucleus as the neuroblastic element of the inter-annular segment.

8th That the cicatricial mass uniting the ends of a divided nerve may be permeated by young nerve fibres from end to end without functional union being effected, if the amount of cicatricial connective tissue present in the mass is sufficient by its pressure to prevent the passage of impulses.

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Plates.

Plate I.

Cruikshank's Preparation, 1776, Hunterian Museum, Glasgow University. Approx. ½ nat. size. View from behind of larynx and trachea of dog. In the middle line is the trachea; on either side of that, the carotid arteries; and the cords furthest out at the sides are the reunited pneumogastric nerves. The ends of the nerves are marked by transfixing bristles, shown in the photograph, and the portion between each pair of bristles is the uniting segment. The right nerve was simply divided, but the left had a portion excised from it, the operation in the former case being 39 days, and in the latter 18 days, before the animal was killed for examination. The dog was perfectly well before being killed. Vide page 2.

Plate II.

Hands of Case I, before operation. Suture of median and ulnar nerves six and a half months after division. Sound hand for comparison.

Shows difference in quality of skin, loss of flexures, atrophy, sore on inner side of first internode of little finger, transverse depressed lines on the nails, and the characteristic attitude.

$\frac{1}{2}$ nat. size.

Plate III.

Hand of Case I, before operation. Lateral view. Shows the position in which the hand was carried at the wrist, lines on nail of thumb, atrophy of the thenar eminence, and part of the cutaneous cicatrix from the wound in the forearm.

½ nat. size.

Plates IV and V.

Hand of Case II with left hand for comparison, after operation. Suture of the median nerve three months after division. Shows the condition of the hand one year after operation. Flexures of palm not so well marked as those of left hand. Shows the restored thenar eminence, and the extent to which the hand can be opened and closed. Where closed the inability to bring the tips of the index and middle fingers by complete flexion of their terminal phalanges into the centre of the palm is displayed. The operation cicatrix is shown in the middle line above the wrist. $\frac{2}{7}$ nat. size.

Plate VI.

Case III. Hand with right hand for comparison. Two months after fracture at the elbow joint, before operation. Shows the position in which the fingers and thumb were carried, and the atrophy of the thenar and hypothenar eminences.
½ nat. size.

Plate VII.
Case III, before operation. Shows the hollowing out of palm and flexion at wrist. $\frac{2}{3}$ nat. size.

Plate VIII.

Hand of Case IV, before operation. Section of ulnar nerve of eighteen months standing. Shows the over extension of the first phalanges of the little and ring fingers, and the atrophy of the hypothenar eminence is also indicated. The transverse cicatrix of the wound above the wrist is also shown. ½ nat. size.

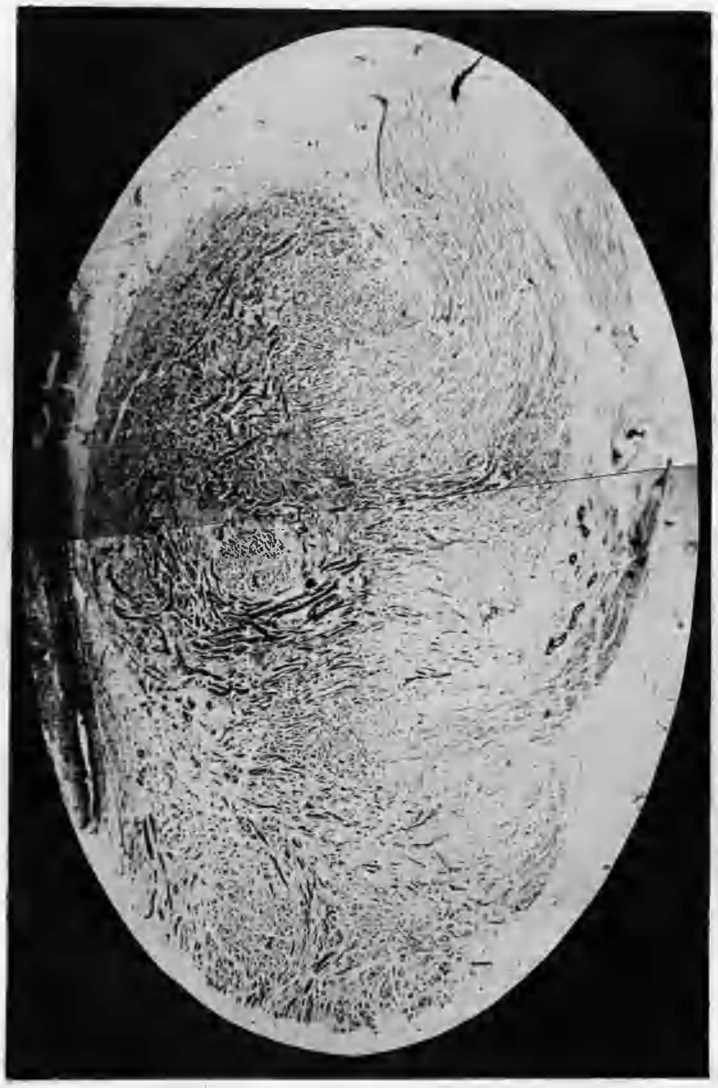

Plate IX.

Longitudinal section of bulb from central end of ulnar nerve six and a half months divided. Case T. Shows nerve curving round at point of entrance at side, and the fibres diverging in bulb. At opposite side of bulb small bloodvessel seen. In bulb the dark streaks and dark points are bundles of young nerve fibres, cut respectively longitudinally and transversely, showing the very irregular course of the young fibres, and the proportion of nerve elements to connective tissue. Zeiss Obj. a_4, Proj. Oc. 2, Camera 22 inches, Magnif. $\frac{10}{1}$.

Plate X.

Longitudinal section of bulb from peripheral end of ulnar nerve six and a half months divided. Case I. (The section is in two halves having been erroneously divided transversely after treatment with Müller's fluid). The lower end in the photograph merged gradually into the nerve stem. The bundles of young nerve fibres are shown as dark lines or dark points, accordingly as they are cut longitudinally or transversely. The more regular longitudinal course is shown in the attached end, and the extremely convoluted course in the free end. The connective tissue appears less dark, and the proportion of this to the nerve tissue is seen to be greater at the free end.

Zeiss Obj. a_1, Proj. Oc. 2, Camera 22 inches. Magnif. $\frac{10}{1}$.

Plate XI

Bundles of young nerve fibres in bulb from central end of ulnar nerve. Case J. From the lower part of section shown in Plate IX. Near centre three small bundles grouped together, and separated by layers of connective tissue, and each containing an enormous number of young nerve fibres, in which are displayed the axis-cylinders, each surrounded by a clear zone. In the upper part of the photograph a bundle appears longitudinally, the fibres showing in parts the delicate axis-cylinder with granular deposit of myeline around, and also oval nuclei. Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.
Cf. Plates XII and XIII.

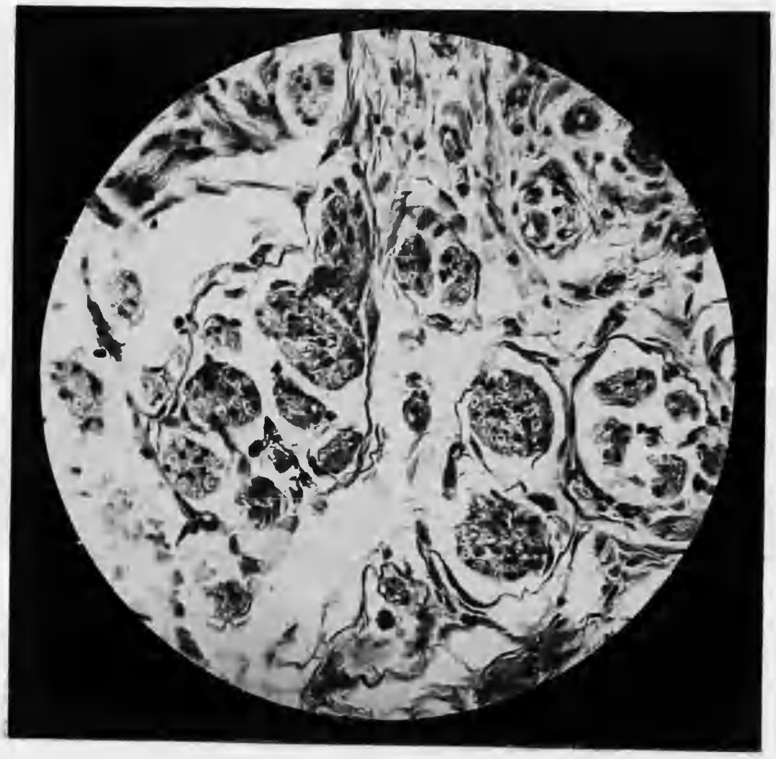

Plate XII.

Bundles of young nerve fibres in bulb from peripheral end of ulnar nerve. Case T. From the free end of section shown in Plate X. Shows the young nerve fibres identical in appearance with those in the bulb from central end (Plate XI.) Many nerve fibres in each bundle. Distinct axis-cylinders. The nuclei in the bundles among the young nerve fibres are displayed. At the upper left hand corner a small portion of a longitudinally cut bundle with its nuclei, and near the centre a bundle obliquely cut.

Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

Cf. Plates XI and XIV.

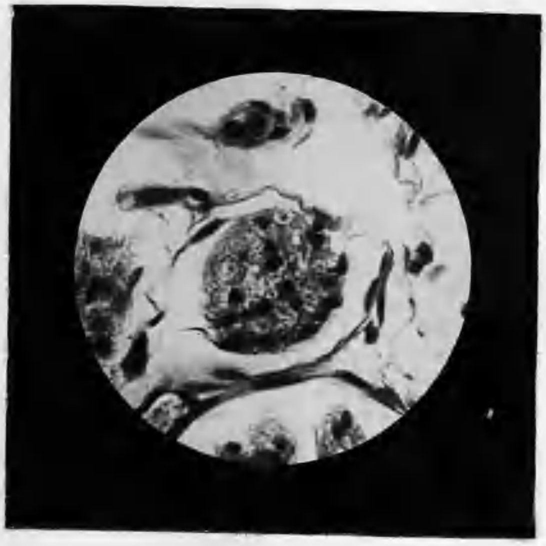

Plate XIII.

Group of small bundles in bulb from central end of ulnar nerve. Case T. Same as shown in Plate XI, but more highly magnified. The upper half of the largest bundle is taking an oblique course; elsewhere, nerve fibres cut transversely. Distinct axis-cylinder in each, surrounded by a well defined clear zone. Zeiss Obj: F, Proj: Oc. 2, Camera 22 inches. Magnif. $\frac{600}{1}$.

Plate XIV.

A bundle of young nerve fibres in the bulb from the peripheral end of the ulnar nerve. Case T. One of the bundles shown in Plate XII, but more highly magnified. Shows young nerve fibres with axis-cylinders, and clear surrounding zone, and many nuclei interspersed within the bundle. Zeiss Obj: F, Proj: Oc. 2, Camera 22 inches, Magnif. $\frac{600}{1}$.

Plate XV.

Longitudinal section showing point of transition from old to young nerve fibres. From the portion of nerve attached to the bulb on central end of ulnar nerve. Case I. (Vide Plate IX.) To the left, a bundle of young nerve fibres less than double the diameter of an old fibre, showing young nerve fibres with delicate axis-cylinders, and granular myeline deposit. Spindle-shaped nuclei attached to sides of young fibres. In the middle of the photograph the old fibre is seen above diminishing as it descends, and giving place to young nerve fibres with spindle-shaped nuclei.

Zeiss Obj. F, Proj. Oc. 2, Camera 22 inches, Magnif. $\frac{600}{1}$.

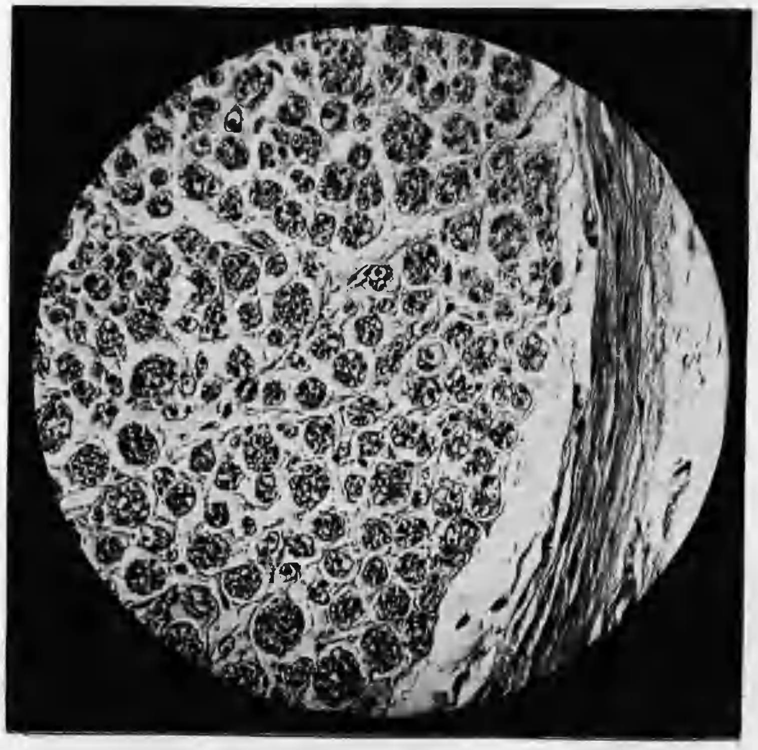

Plate XVI.

Transverse section of ulnar nerve immediately proximal to the bulb on the central end. Case IV. Nerve eighteen months divided. Portion of a fasciculus. Shows normal perineurium. Small bundles of young nerve fibres, arranged like single old fibres. In some a delicate sheath surrounding the bundle.

Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

Plate XVII.

Transverse section base of cone from peripheral end of ulnar nerve. Case IV. Shows compact tissue with small bundles of young nerve fibres cut transversely. Nuclei are seen in the bundles in addition to nerve fibres.
Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

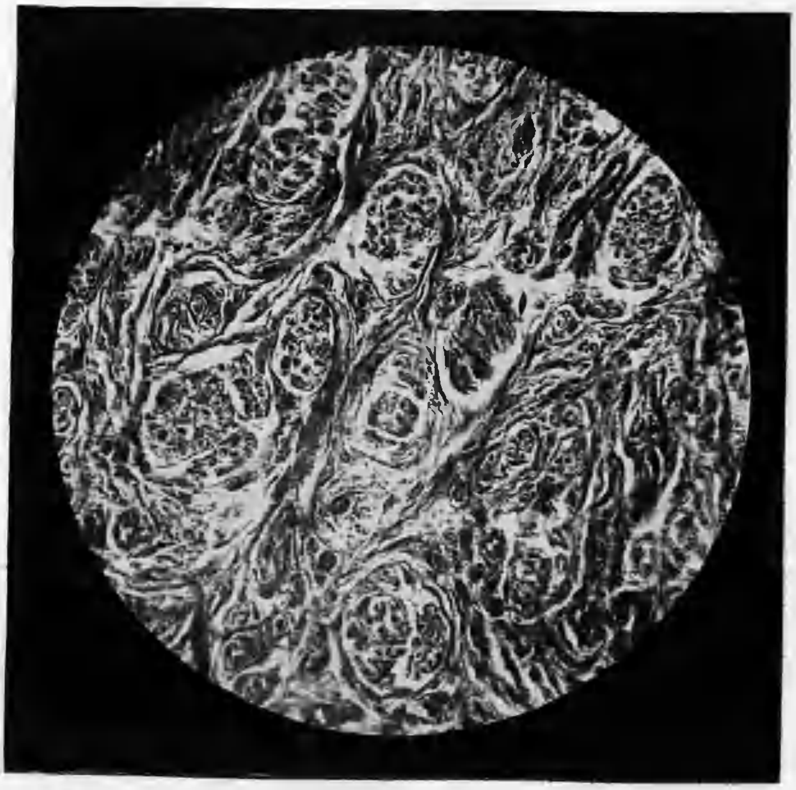

Plate XVIII.

Transverse section proximal end of intercalary segment uniting ends of median nerve. Case I. Shows compact tissue. Dense groundwork of fibrous tissue, containing in its meshes bundles of young nerve fibres showing nuclei.
Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

Plate XIX.

Transverse section: distal end of intercalary segment uniting ends of median nerve. Case T. Shows dense masses of cicatricial connective tissue in the lower half of the section, with a few transversely cut bundles of young nerve fibres, and one bundle running longitudinally in the upper half.

Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

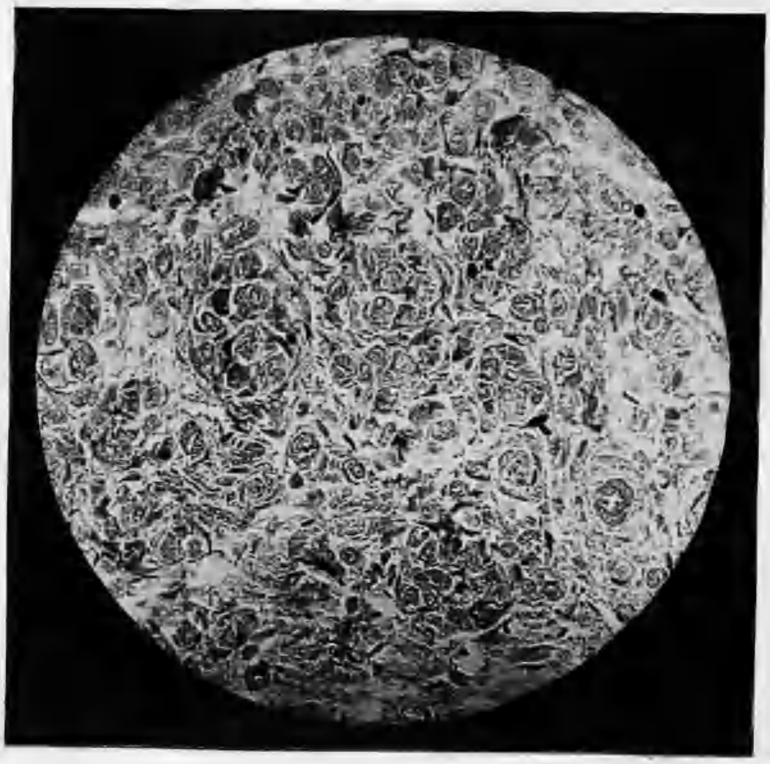

Plate XX.

Another portion of the same transverse section showing large numbers of very small bundles of young nerve fibres.

Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

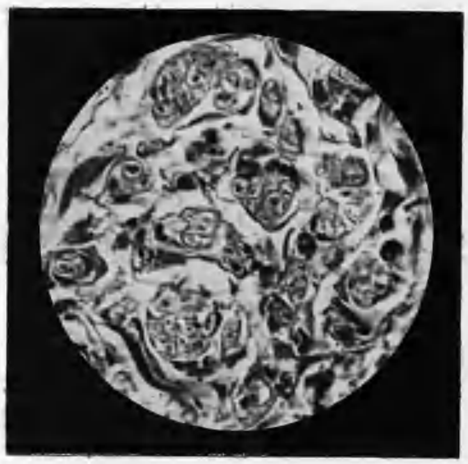

Plate XXI

Longitudinal (Radial) section through intercalary segment uniting ends of median nerve. Case I. A portion at the centre of the segment. Shows several bundles of young nerve fibres cut transversely. Zeiss Obj. F, Proj. Oc. 2, Camera 22 inches, Magnif. $\frac{600}{1}$.

Plate XXII.

Another portion of same longitudinal section, also at the centre of the segment. Shows a bundle of young nerve fibres longitudinally. Some of the fibres show the axis-cylinder, and all show the commencing myeline sheath.
Zeiss Obj. F, Proj. Oc. 2.
Camera 22 inches, Magnif. $\frac{600}{1}$.

Plate XXIII.

Transverse section proximal end of portion excised from the median nerve. Case III. Nerve compressed at seat of fracture. To show the normal subdivision into fasciculi and for comparison with Plate XXIV. Cf. Plate XXV for higher magnification.
Zeiss Obj. a_1, Proj. Oc. 2
Camera 22 inches, Magnif. $\frac{10}{1}$.

Plate XXIV.

Transverse section of distal end of portion excised from the median nerve. Case III. Nerve compressed at seat of fracture. To show normal subdivision into fasciculi. The epineurium is only partially shown, as the sections were taken from the extreme end of the nerve, and the epineurium had retracted, leaving the individual fasciculi projecting.
Cf. Plate XXVI for higher magnification.
Zeiss Obj. a_1, Proj. Oc. 2.
Camera 22 inches, Magnif. $\frac{10}{1}$.

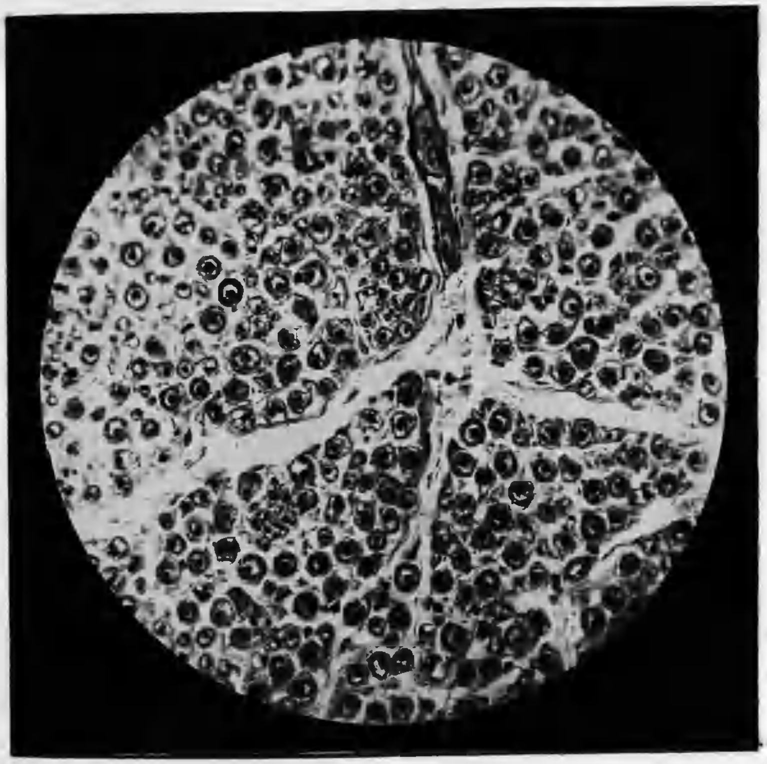

Plate XXV.

Part of a fasciculus from proximal end of portion excised from median nerve. Case III. Nerve compressed at seat of fracture. Shows old myeline nerve fibres. Appearance same as that of section of normal nerve, treated by same methods.

Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

Plate XXVI.

Part of a transversely cut fasciculus from the distal end of portion excised from median nerve. Case III. Nerve compressed at seat of fracture. Shows normal perineurium; no old myeline nerve fibres; but instead small bundles of young nerve fibres, grouped as the single old fibres in the preceeding photograph, and many of the bundles about the same size as an old fibre. Among the young fibres nuclei are seen, and surrounding the bundle in many cases a delicate sheath. Zeiss Obj. D, Proj. Oc. 2, Camera 30 inches, Magnif. $\frac{340}{1}$.

Plate XXVII.

Transverse section of portion excised from musculo-spiral nerve. Case III Through point of transition from old to young nerve fibres. Near the centre are two very large old fibres the lower of which shows a slight thickening at one side representing a nucleus and protoplasm of the sheath of Schwann, while the upper shows at one side a large nucleus with two young fibres at its side, all three structures lying between the myeline sheath and sheath of Schwann.
Zeiss Obj. F, Proj. Oc 2, Cam. 22 inch, Magnif. $\frac{600}{1}$.

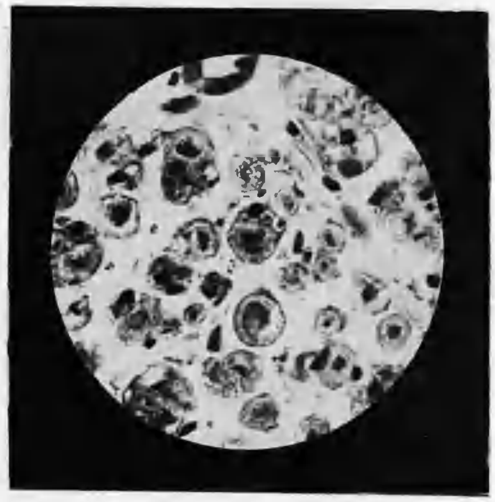

Plate XXVIII.

Same section. Portion of perineurium shown to the right. Near centre, a bundle of young nerve fibres with two nuclei, and the old myeline sheath and axis-cylinder at one side.
Same magnification.

Plate XXIX.

Same section. Perineurium at right hand side. Near centre a bundle of young nerve fibres with merely traces of old fibre at one side.
Same magnification.

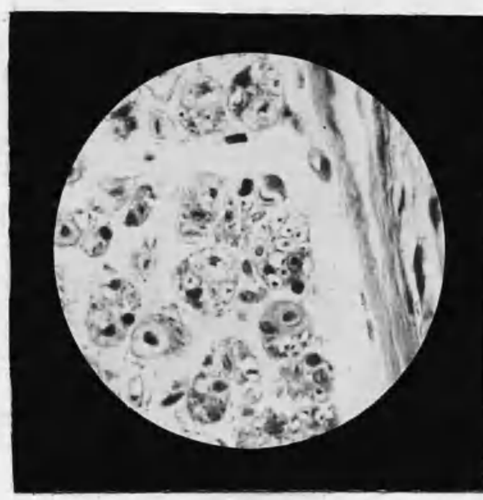

Plate XXX.

Longitudinal section through point of transition from old to young nerve fibres. From portion removed from musculo-spiral nerve. Case III. Two old fibres are seen descending in the middle of the plate, terminating and giving place, each to a bundle of young nerve fibres. Both old fibres display the bulbous termination of the axis-cylinder.

Zeiss Obj. F', Proj. Oc. 2, Camera 22 inches, Magnif. $\frac{600}{1}$.