Nerve-suturing (neurorrhaphy) : degeneration and regeneration following section : microscopical appearances : one of the Mütter course of lectures delivered before the Philadelphia College of Physicians / by De Forest Willard.

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NERVE-SUTURING (NEURORRHAPHY):

DEGENERATION AND REGENERATION FOLLOWING SECTION; MICROSCOPICAL APPEARANCES.

One of the Mütter Course of Lectures delivered before the Philadelphia College of Physicians.

BY

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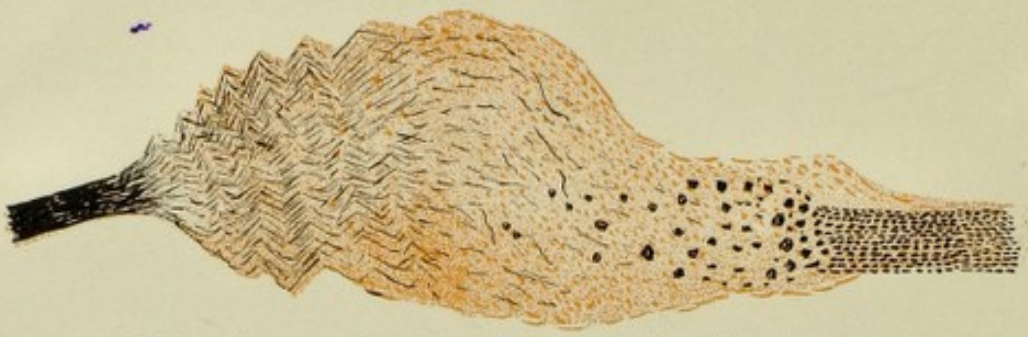

FIG. 1.—Nerve-resection; suture; left nerve. (Experiment No. I.)

FIG. 2.—Nerve-resection; suture; right nerve. (Experiment No. I.)

FIG. 3.—Nerve-splicing; left nerve. (Experiment No. VII.)

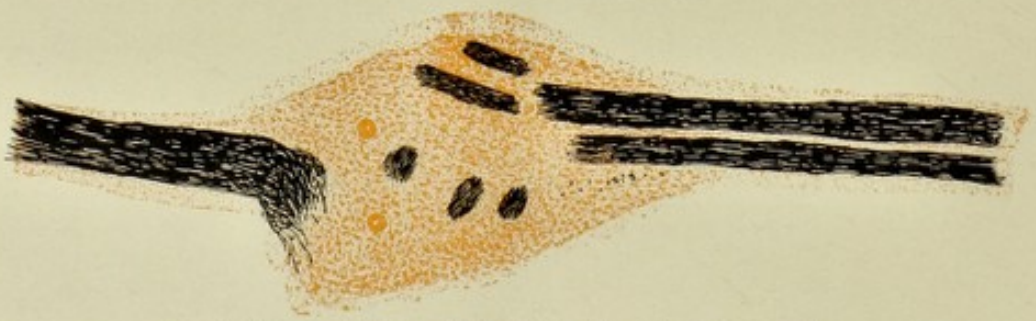

FIG. 4.—Nerve-splicing; right nerve. (Experiment No. VII.)

NERVE-SUTURING (NEURORRHAPHY): DEGENERATION AND REGENERATION FOLLOWING SECTION; MICROSCOPICAL APPEARANCES.

THE surgical treatment of affections of the peripheral nerves owes its prominence very largely to the fact that the general practitioner and the neurologist, into whose hands many of these cases fall, find themselves at times utterly helpless in the management of diseases of this class, and the surgeon is called upon for aid. Unfortunately, surgical measures are by no means always successful; but immense advances have been made during the past decade in diminishing the number of unsuccessful cases operated upon.

The most striking revolution in the pathology of the nerves took place about one hundred years ago, when Cruikshank taught that nerves do not always degenerate when cut, but that they are sometimes restored after section. During the last thirty years much has been done to point out the surgical means by which wounded and degenerated nerves may be repaired. Unfortunately, on the one hand, nerves fail to unite when left to themselves after injury, and, on the other hand, sometimes show a wonderful persistency in uniting when for any cause they have been excised.

A severed nerve degenerates; the peripheral portion begins to undergo the retrograde change throughout its entire length within from twenty-four to forty-eight hours after the injury has been received. The best observers are now opposed to the belief that this process starts at the cut end and spreads downward. The changes observed are the destruction of the myeline, the multiplication of the nuclei, and the loss of continuity of the axis-cylinder. Marked atrophy is observed in the course of two or three weeks. The microscopical appearances in nearly all of these cases show that the axis-cylinder as well as the myeline in the distal portion has degenerated. The proximal end undergoes little change. Observations show that the myeline, instead of becoming broken into large fragments which subsequently become smaller, as in the peripheral end, is rapidly reduced into fine granules, which later on assume a yellowish-brown color with osmic acid. The nuclei multiply and increase in size.

In order to test more perfectly the different methods of nerve-suturing,

to give the procedures a fair trial, and to observe the microscopical changes, I have during the past summer experimented upon a number of dogs, of which the following is but the partial summary of results. In all of the experiments the part to be operated upon was cleanly shaven, the skin thoroughly scrubbed with soap, brush, and water, then with bichloride, and the area protected with bichloride towels. The instruments and the hands of the surgeon received the most careful attention. The wounds were washed with from 1–1000 to 1–2000 bichloride solution and closed, sometimes with catgut drainage, but usually without any drainage. Ether was used in each case.

From my experience with dogs I am very decidedly of the opinion that it is impossible to secure thorough antisepsis with the care which it is possible to obtain from ordinary attendants. The wounds were dressed with iodoformized collodion, but to retain an antiseptic dressing is impossible in most of the regions of a dog's body. The persistent and indefatigable efforts which most of these animals exhibit to displace and remove the bandages are prodigious. In the limbs encasement by gypsum bandages is sometimes advantageous. I believe, therefore, that the tongue of a dog, applied, as it usually is, with such constant frequency to a wound, offers ordinarily as good hope of quick recovery as can be obtained under poorly-maintained asepsis. With perfect laboratory arrangements, of course, asepsis is possible, but these surroundings are ordinarily unattainable.

Experiment No. I.—Nerve-resection: suture. Black pup. The region over the sciatic nerve posterior to the great trochanter was rendered thoroughly aseptic as above described. An incision was made dividing the fibres of the muscle longitudinally, and one-quarter of an inch of the nerve was resected. The divided ends were stitched with fine chromicized catgut, using a round sewing-needle, the ends of the nerve being purposely left a quarter of an inch apart. The sutures were introduced crossing each other at right angles. The nerve was disturbed as little as possible. The muscles and skin were sutured separately, and the wound was cleansed and closed with iodoformized collodion.

On the following day I was astonished to find that the dog was able to walk and even to skip about, apparently having but little concern about the operation, although I was certain that I had divided the entire nerve. Subsequent events proved, however, that a portion of it had been left uncut.

The next day under ether I removed three-quarters of an inch of the left sciatic, dividing also the branch which ran to the gluteal muscle. A compact bundle of four strands of catgut was stitched between the two ends, thus bridging the gap for the original distance of three-quarters of an inch. The wound was closed as on the other side.

On the fourth day there were no signs of suppuration on either side. The wound on the right side appeared to have united by first intention.

On the ninth day the wound on the right side was almost entirely healed, being covered only with a slight scab. There was no paralysis on the right side, no drop of the foot or toe. The limb was apparently almost normal. On the left side there was paralysis of the extensors of the toes, and the pup was walking upon the dorsum of the foot,—that is, in a condition of extreme equinus, though the limb was well handled and the animal was able to run quite briskly, save for the toe-drop alluded

to. Beneath the wound on the left side was a quantity of serum, which was pressed out, but there was no pus. The wound was washed out with bichloride solution, 1–2000, and thoroughly cleansed. Catgut drainage was instituted and the wound was covered with iodoformized collodion.

On the twentieth day the animal was perfectly well in the right leg; on the left side he was walking upon the dorsum of the toes.

On the twenty-fourth day both wounds were perfectly healed. The pup was frisky, gambolled about, and walked on the soles of both feet. One would scarcely detect that an operation had been performed upon him. He was a young dog, and this may account for his having done so admirably.

He continued well, and was killed on the forty-sixth day. On the right side at the line of division, the cicatrix, skin, and superficial tissues were firm and healthy. The site of the operation upon the nerve was distinguishable only by a slight enlargement, and to the naked eye there had been apparently perfect union. On the left side the bundle of catgut had disappeared; the cicatrix was firm and thoroughly healed. The upper end of the lower fragment had wandered, and finally attached itself upon the under surface of the biceps, half an inch below the trochanter. The end of the upper fragment was bulbous, and lay behind the trochanter in a bed of connective tissue.

Microscopical Examination.—Weigert's and Pal's stains were used. *Left Nerve* (Fig. 1).—Upper fragment terminates in a bulb of fibrous tissue which contains numerous nerve-fibres radiating like a fan from the termination of the nerve-fibres. The sheath is continued into the fibrous tissue of the bulb, being considerably thickened before the new fibres split up. Scattered through the fibrous tissue are numerous nerve-fibres, making their way towards the lower fragment. Below are seen drops of degenerated myeline in several spots. The lower fragment also shows beads of degenerated myeline. (Examinations by Dr. W. S. Carter.)

Right Nerve (Fig. 2).—Apparently there is a continuity of nerve-fibres as viewed with the naked eye. The microscope showed that only one division or bundle of the nerve had been severed. The cut division had separated half an inch and was united by fibrous tissue, scattered through which were found many new nerve-fibres.

Experiment No. II.—Nerve-splicing. Young Scotch terrier. Technique as above described. Half an inch of the right sciatic nerve was removed, the two ends split longitudinally for one-quarter of an inch, and flaps cut on opposite sides from each other. These flaps were then turned upon their bases and sutured. Two chromicized catgut sutures were used. The muscles and skin were sutured and the wound was closed with iodoform collodion.

On the third day the dog was walking about, but with a tendency occasionally to place the dorsum of the foot upon the ground instead of the plantar surface, as described in Experiment No. I.; otherwise the movements of the limb were normal. The wound had apparently united, and was healing kindly.

On the ninth day the left sciatic was divided one inch below the trochanter, the nerve being reached through the muscle. It was divided and united by chromicized catgut.

On the tenth day the first wound was nearly closed, although there were a few granulations at the lower extremity, but the dog was able to stand upon and to walk with the leg operated on the day before.

On the fourteenth day after the first operation both wounds were doing well. When the animal walked there was no apparent paralysis, but on running and frisking he ran upon three legs, the limb operated upon the second time being apparently shorter, but not paralyzed.

On the twentieth day the dog was walking about apparently with perfect ease and with no paralysis. Sensation was tested with a pin, but the results were uncertain.

The animal was killed on the forty-seventh day after the first operation. The silk-worm sutures in the skin were found *in situ;* the left nerve lay in its proper position. The line of union was well marked, only slight enlargement being noticed. At the site of operation the nerve was adherent to the muscle on one side, but could be dissected off cleanly on the other side. On the right side (the first operation) there was a firm cicatrix extending down to the nerve. The nerve at the seat of operation was firmly adherent to the fascia and muscle beneath. The visible ends of the nerve were apparently separated about two lines, and had slightly deviated in their course.

Microscopical Examination.—Left Nerve.—The fibres coming from above split up into a great number of fibres radiating like a fan. Below this there is about three-eighths of an inch of fibrous tissue containing small fibrils running in all directions. In this fibrous tissue many black drops of degenerated myeline are found. On the lower end of the section the degenerated myeline is all grouped together, and not scattered through fibrous tissue.

Right Nerve.—Upper end splits up into small fibrils which run in all directions in the fibrous tissue. Throughout the fibrous tissue are seen nerve-fibres running in all directions and many drops of all sizes of degenerated myeline. Apposition has not been end to end, but there has been some overlapping. No continuity of fibre can be seen in section.

Experiment No. III.—Nerve-resection. Yellow Scotch terrier; young. Technique as before. Three-quarters of an inch of the left sciatic was cut out and removed, the removed piece being at once re-inserted and sutured in position, the four ends being united with fine catgut.

On the fifth day the animal was in good spirits and walking without paralysis, but apparently the leg was a little sore.

On the tenth day the skin sutures had given way, but the wound was clean and nearly closed by granulation-tissue.

On the fourteenth day the wound was closed except for a small ulcer at one end. He was walking without difficulty, and without paralysis, except when running.

On the twentieth day the dog could stand on his leg only occasionally, showing a little tenderness.

On the twentieth day a second operation was performed similar to that which had been done upon the right sciatic, the removed piece being at once sutured in position. One week later both wounds were perfectly healed.

The dog was killed on the forty-fourth day after the first operation. The skin was thoroughly healed, and there were no signs of suppuration. The sciatic at the seat of operation was bulbous with thickening about the line of union, while between these two bulbous portions was a bridge about one-half the size of the original nerve.

At the seat of the second operation there was thickening of the connective tissue extending for three-quarters of an inch, and included the graft at the upper and lower ends of the nerve. There was apparently firm and continuous union.

Experiment No. IV.—Nerve-flap splicing. Black Newfoundland dog. Half an inch of the right sciatic was cut away, and the nerve slit for a half-inch, commencing one-quarter of an inch from the end. Flaps were then cut upon the opposite sides, turned and sutured end to end, leaving the original ends three-quarters of an inch apart. Three days later the wound had entirely healed. The dog was walking with paralysis of the extensors of the toes and on the dorsum of the foot, in a condition of extreme equinus.

He was killed on the twenty-fifth day by chloroform. The nerve was found in proper position and adherent to the cicatrix. The continuity of the nerve was apparently entirely restored. Around the nerve was marked thickening throughout the extent. Above and below the calibre appeared to be slightly narrowed.

Experiment No. V.—Nerve-resection. Catgut bridge inserted. Small bitch pug. Technique as before. Three-quarters of an inch of the right sciatic was removed and a bundle of four strands of catgut was sutured in position. The wound was dressed as before.

On the tenth day the silk-worm skin-stitches had nearly cut through, being removed by the dog. The wound had opened and the dog was quite lame, apparently from soreness. She could walk, but the toe dropped.

On the eleventh day she was feverish and refused food, and was killed on the fourteenth day, as she was losing flesh rapidly.

Small patches of miliary tubercle were found throughout both lungs, which evidently had existed previously to the operation, as it was noticed that the animal was in poor flesh and spirits. The nerve above and below the point of section for a quarter of an inch was removed. No appearance of the catgut bridge was visible, it probably having been removed after the wound opened. There was but a slight connective-tissue bridge. The wound was still open.

Microscopical Appearances.—Upper fragment terminates in connective tissue, the nerve breaking up into fibrils. Below this there is about an inch of fibrous tissue containing groups of fibres here and there, in which the myeline is in drops showing advanced degeneration. A few muscle-fibres are found in the connective tissue. No undegenerated fibres could be found in this mass of connective tissue.

At the lower end of the section the bundle of nerve-fibres are all grouped together, and show a beaded condition of the myeline, but apparently the degeneration is not so far advanced as that seen above.

Experiment No. VII.—Nerve-splicing; large bitch pug, old and very fat. The left sciatic was divided, and three-quarters of an inch of the nerve removed. The nerve was then slit longitudinally and the flaps turned upon their bases. One tore out and left only the upper half of the flap. This, however, was turned downward, and stitched to the upper slit half of the lower fragment.

Nine days later the wound was perfectly healed and the animal was running with ease and comfort; the toes dropped, however, and she stepped upon the dorsum when attempting to run rapidly.

Three-quarters of an inch was removed from the right sciatic, and the nerve thoroughly cleared, stitched, and sutured end to end. On the next day the animal appeared heavy and feverish, and refused water. The weather was extremely hot. The animal was very old, and on the following day, without any assignable cause, was found dead in the kennel. There were no symptoms of tetanus.

At the seat of the first operation (left) there was an irregular connective-tissue bridge, but the point from which the flap was taken had become bulbous. The flap

which had been sutured showed drops of degenerated myeline, the lower nerve had become loosened, and there was irregular union. One-half of the lower fragment, which had remained undisturbed, was normal, but the other half showed signs of degeneration.

On the other side (right) the stitches were firmly in place. There was already an attempt at union, although the operation had only been done twenty-four hours. Neither upper nor lower fragments showed any change, as the time had been but two days. There were numerous small bundles of nerve-fibres which had been cut across as they lay in the new bridge of connective tissue.

Microscopical Study.—Left.—Fibres terminate abruptly in the great mass of fibrous tissue without breaking up. In this great quantity of fibrous tissue are found many patches of degenerated nerve-structure. Below the fibrous tissue—*i.e.*, upper end of lower segment—the fibres are beaded, surrounded by sheath. Degeneration here is not as far advanced as in some of the other specimens. (Fig. 3.)

Right.—No continuity of fibres demonstrable. A few bundles evidently cut in different planes. There is no splitting up of fibres and no degeneration. (Fig. 4.)

Experiment No. IX.—Resection of nerve; catgut bridge; black mongrel. Three-quarters of an inch of the right sciatic resected, and a bundle of eight strands of sublimated catgut wrapped together was stitched into the gap. On the eighth day the wound was nearly closed. The dog was walking, only occasionally dropping his toes and walking on the dorsum of the foot; otherwise he was without signs of paralysis. The animal was chloroformed and killed on the thirty-fifth day. The cicatrix was firm and healthy. The nerve was not united to the cicatrix. The divided ends were separated one inch. The upper fragment was enlarged and thickened, lying just behind the trochanter, and the connective scar-tissue around the lower fragment had retracted so that each had attached itself to the outer face of the semimembranosus. The band between the two ends was evidently connective tissue.

Microscopical Appearances.—Union is not in direct line but overlapping. Just below this point of apposition there are many spots stained black, but can find no nerve-fibres in these spots. This mass of connective tissue contains fat in large quantity and some muscle-fibres. Below the mass of connective tissue are found nerve-fibres degenerating.

Experiment No. XI.—Resection; insertion of another nerve; grafting; black and white setter. Resected three-quarters of an inch of the sciatic. Into this gap was immediately inserted seven-eighths of an inch of the sciatic nerve of another dog, removed under anæsthesia, while the animal was living, the second animal being then killed for another purpose. The nerve was reached through the intermuscular space behind the trochanter. The graft was stitched at either end by catgut. Six days later the wound had opened the entire extent. The animal was doing badly, and the weather was exceedingly hot; but under care, feeding with bread and milk, and removing to an open pen, the animal soon improved, and a week later was walking with only an occasional dropping of the toe and stepping upon the dorsum of the foot, but at other times the leg was moved with apparent ease. He was killed on the thirtieth day. The lower end of the upper fragment was firmly adherent to the tissue over the trochanter, the cicatrix of the integument having been brought forward and made adherent to the trochanter. The upper end of the lower fragment

FIG. 5.—Nerve-grafting; bridge of ivory; right nerve. (Experiment No. XIII.)

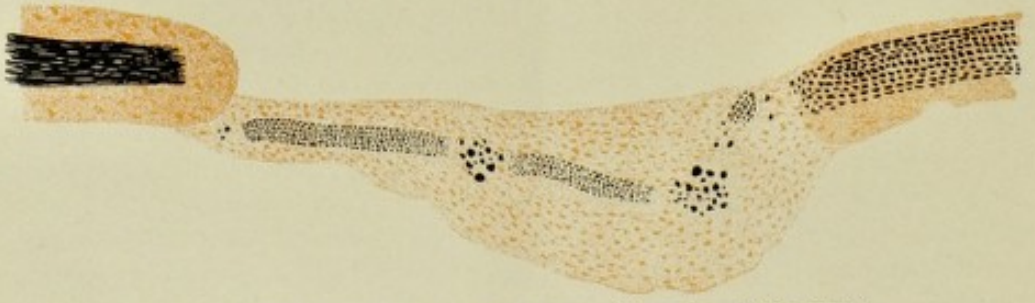

FIG. 6.—Nerve flap-splicing; right nerve. (Experiment No. XIV.)

lay between the trochanter and the tuberosity of the ischium and was connected with the upper portion by a small bridge from the latter which merged into it.

Experiment No. XII.—Decalcified bone-tube splicing; old, black, Newfoundland dog. Three-quarters of an inch of the right sciatic nerve was resected. The ends were then drawn one-third of an inch into a decalcified-bone tube inserted into the gap, and carefully stitched *in situ.*

On the tenth day the dog seemed sick, and was losing flesh, and, as the dorsum of the foot was becoming ulcerated from pressure in walking with his toes dropping, he was killed.

The ends of the nerve were found adherent to the cicatricial tissue in the intermuscular space. The bone tube had entirely disappeared, but the loops of catgut which had been passed through the eyes of the tube were plainly visible, showing that it had not been pulled from the wound by the dog, but that it had been absorbed. The wound was entirely healed, and there were no signs of suppuration at any point.

Experiment No. XIII.—Nerve-grafting; bridge of ivory; yellow and white bitch beagle. Three-quarters of an inch of the right sciatic was removed, and a small piece of ivory of the same length, bored at each end, was inserted and stitched with catgut suture.

On the fifth day the wound had nearly closed, and it had entirely united on the ninth day. The dog was in excellent condition. He was walking without discomfort, and only occasionally upon the dorsum of his foot; otherwise motions were normal.

He was killed by chloroform on the thirty-second day. The wound was perfectly closed, and there were no signs of suppuration. The piece of ivory was found encysted and lying in the connective tissue on a plane one-quarter of an inch superficial to the plane of the nerve. The nerve-ends had separated three-quarters of an inch and were united apparently by fibrous tissue.

Microscopical Examination.—The nerve terminated abruptly in a bulb of fibrous tissue, several bundles being cut off obliquely. At the lower end of the connective tissue there is a group of black-stained drops of degenerated myeline, surrounded by a capsule of fibrous tissue. In the diagram (Fig. 5) are shown the nerve-fibres, some of them bulbous at the end, others lobulated or beaded. Some are shrunken, some enlarged.

Through the fibrous bridge are seen numerous radiating and developing nerve-fibres. While apparently straggling and without continuation, yet this may be due to improper section in preparation. Their presence shows the attempt at reunion and transmission of influence might have been perfected later.

Experiment No. XIV.—Nerve-flap splicing; black Newfoundland dog. One and a half inches of the right sciatic resected. Flaps cut from the ends, turned over, and united with catgut sutures, the flaps being end to end. Killed by chloroform on the twenty-eighth day.

Microscopical Appearances.—An irregular connective-tissue bridge connects the nerve-ends, in which are found beaded and degenerating remains of the nerve-flaps. At several points aggregations of degenerating myeline are also seen. The upper fragment does not show any attempt to send out the fan-like projections of nerve-fibres before noted. The lower fragment is degenerated. (Fig. 6.)

In Experiment I. it will be noticed that the sciatic nerve was severed, and the next morning the animal was walking about with great ease without the slightest paralysis. That union of the nerve occurred in this time I could not believe, and subsequent examination showed that a portion had been left uncut. Unfortunately, I did not see the dog after he recovered from the ether, and do not know whether he walked at once.

In cases where portions are excised, rapid union may take place by means of multiplication of the sheaths, if there is but little fatty degeneration of the peripheral ends. Experiments seem to prove not only that transmission of nerve-force is possible to be secured, but that degeneration is also prevented by suturing.

Gluck's experiments show that union in a fowl is much more rapid than in a rabbit, and more rapid in the rabbit than in the dog; therefore, in man even greater delay may be expected. Clinical facts prove that there are instances of nerve union in seventy hours in the fowl, while in man restoration is not accomplished for several weeks.

It is but seldom, fortunately, that we have an opportunity for examination, microscopically, of the effect of nerve-section in man within the first few weeks, and results, therefore, must be determined by symptoms. We are justified, however, in believing that union has occurred in the continuity of a divided nerve when there is restoration of sensation, absence of atrophy of the muscles, and the presence of contractility. Clinical records show most decidedly that union does and may be expected to occur. An inch may be excised with the expectation of good results in from six to twelve months. Clinical facts prove that the views formerly entertained by neurologists in regard to nerve-union are wrong, and that with the speedy repair obtainable by antiseptic methods reunion and regeneration are possible. Certainly we can hope for good results with care and attention to detail, and by accurate approximation of the divided nerve and retention by fine catgut sutures.

Suture of a nerve after many months of separation of the divided ends may result in restoration of the functions, even if there is no resultant continuity of the axis-cylinders; to apply one axis-cylinder absolutely to its original is impossible. Even if no nerve-union takes place, nerve-regeneration seems slowly to occur, as axis-cylinders are formed, with later deposit of myeline, as has been accurately described by Neuman.

Howell and Huber,[1] in a careful and most comprehensive study of the subject, have entered into the physiological, histological, and clinical study of both regeneration and degeneration of nerves.

Their investigations were undertaken especially to learn, first, whether union and return of function of severed nerves without degeneration of the distal portion is possible, and, secondly, whether union is possible with return of function between the central portion of any one special nerve and the

[1] Journal of Physiology, 1892, vol. xiii. No. 5 (Mitchell Prize Essay).

distal portion of another of opposite function. They have traced the various experiments from Cruikshank in 1795 to the present time, and point out the errors of interpretation in various experiments.

In regard to pseudo-motor activity of sensory nerves they offer only the explanation of Heidenhain, that it is caused by an increased secretion of lymph, which acts as a stimulus to the partially-destroyed plates of the muscle-fibres, as, for instance, through the chorda tympani fibres of the lingual. They believe also that the experiments of Reichert and Schiff need further confirmation, as sources of error in interpretation are quite possible. They conclude that although the peripheral end of one spinal nerve can unite with the central end of another with return of function, yet that there are no completely satisfactory experiments showing that a pure motor trunk can unite with a pure sensory trunk with return of function to the peripheral portion. They agree with many observers that the myeline disappears after section, and that segmentation begins simultaneously throughout the peripheral end, in accordance with the testimony of the majority of investigators. The preponderance of evidence seems to be on the side of those who hold that the axis-cylinder degenerates along with the myeline.

If we accept the modern view that the axis-cylinder is an enormously elongated process of a nerve-cell, it would follow as a matter of course that this process when severed from its parent cell must degenerate. As to the process of degeneration of the primitive sheath, they are not able to state accurately.

Union by first intention, simple and absolute, end to end, without degeneration, cannot be proved; but immediate and rapid return of function has certainly been demonstrated too often for its possibility to be denied. Whether this immediate return is through direct transmission across the minimum amount of space, or whether the restoration of the parts to their normal positions in some way assists other trunks in taking up the function of the injured nerve, is still uncertain.

Those who maintain that new axis-cylinders arise directly from the old ones of the central end have never been able positively to demonstrate their belief.

Their conclusions are:

1. That primary union of a nerve without degeneration of the peripheral end does not occur.

2. The time of degeneration varies, complete loss of irritability being usually present in from two to four days in dogs, showing that the degenerative process commences early.

3. The return of irritability and conductivity in a peripheral end after union was noticed at the end of twenty-one days, and it varies at later periods of time, being nearly complete in the majority of cases at the end of eleven weeks. This return of function begins first in the neighborhood of the wound and extends slowly centrifugally, although the branches do not improve in regular anatomical order.

4. Return of sensation antedates that of motion, as has been frequently noted by other observers.

5. Mechanical stimulation is sometimes more effective than electrical in producing reaction.

Their experiments upon dogs were chiefly upon the median and ulnar nerves. Their work did not come under my observation while I was experimenting, and I selected the sciatic for my purposes of study, with the result that paralysis occurred more frequently and was more noticeable than would have been the case in the front leg of an animal. A dog gets on very well with two hind legs and one front one. They examined their nerves by teasing, not by section, and found that degeneration occurred simultaneously throughout the entire extent of the distal segment.

Etzold shows that regeneration begins at the central end and travels slowly down the course of the nerve.

Howell and Huber report that of eighty-four primary sutures forty-two per cent. were successful, forty per cent. improved, and eighteen per cent. received no benefit. Howell criticises the reports of Bowlby and of Gluck in the so-called cases of primary union, since no careful electrical tests were made.

Arloing and Tripier have shown that rapid return of sensation can occur without union, and that the movements of muscles can be executed without the presence of the nerve immediately distributed to the muscle.

In two cases of so-called primary union, one by Bramwell, the hand was at once examined and there was no loss of sensation or motion. It was attributed by the surgeon to the fact that nerve impulse could pass when the ends were in close apposition, just as an electrical current can pass by contact. But it has been very definitely proven by physiologists that nerve-impulse cannot travel when the axis-cylinder is interrupted.

In Kraussold's case return of motion and sensation was very rapid: within forty hours impulses were transmitted, although union could scarcely have taken place in this time.

Reichert[1] published interesting demonstrations upon regeneration of nerves. While sensory fragments frequently unite with sensory fibres and motor fibres with motor fibres, he attempted to change the function of a nerve by resecting it and uniting the vagus and hypoglossus.

Vulpian and Rosenthal had attempted to unite the motor fibres of the hypoglossus with the sensory fibres of the lingual, but they did not obtain union of the sensory with the motor fibres.

Vulpian and Philippeau[2] united the central end of the vagus with the peripheral end of the hypoglossus, but did not find any properly-regenerated fibres in the hypoglossus trunk, or other normal nerve-fibres in which the

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[1] American Journal of the Medical Sciences, January, 1885.

[2] Lancet, September 21, 1878.

medullary sheath was developed ; they regarded regeneration as independent of reunion.

Other experiments have been undertaken to show that after regeneration of nerves the different trunks which were united in the animals were still able to perform their original co-ordinate movements.

Reichert had the hypoglossus cut close to its exit from the cranium and the vagus at the thyroid. The peripheral end of the hypoglossus was sutured with silk to the central end of the vagus. Microscopical examination later of the hypoglossus trunk showed that it contained degenerated fibres and a large number of small fibres in the medullary sheath, proving that the motor fibres of the vagus had actually become united to similar filaments of the hypoglossus, and that the hypoglossus fibre conveyed impulses which were peculiar to the vagus. In one case he found that sensory-fibre irritation of the hypoglossus trunk produced effects like those induced by excitation, thus showing that motor and sensory nerves can convey impulses peculiar to another motor or sensory nerve of entirely different function. He calls attention also to the fact, as shown by Bert's experiments, that sensory fibres can convey impressions in both directions. This Bert proved by grafting the tail of a rat upon the animal's back, and, after union had occurred, severing the tail from its normal connection and then transmitting sensation in the reverse direction.

With regard to the process of regeneration which takes place in favorable cases after division and regeneration of a nerve, there has been a difference of opinion among investigators. Korybutt-Daskiewicz[1] has described it thus: "After liquefaction of the old medulla in the central end there occurs the formation of new myeline with the peculiar appearance that between the two former constrictions one or two new ones are formed. The nuclei of the sheath of Schwann also undergo changes in the central end near the division of a nerve; they swell up, become surrounded by granular protoplasm, and, after becoming separated from the fibres, assume an elongated form, whether finally developing into nerve-fibres cannot be definitely ascertained. The axis-cylinders in the peripheral part break up into more or less numerous fragments during segmentation of the medulla, and of these some apparently liquefy and participate in the same changes as the myeline, while others persist and clothe themselves with a new medullary sheath. Before the degeneration of the myeline begins to lessen, the fragments of the axis-cylinder commence to lengthen in each direction, and the nuclei existing within the sheath begin to elongate and lie at certain distances from each other. Simultaneously with this process the new medullary sheath makes its appearance as a varicose or uniform deposit upon the axis-cylinder. Thus the fragments of the axis-cylinder remaining serve as a starting-point for a new endogenous formation of nerve-fibres. They present no tendency to blend with one another, but remain in contiguity, grow-

[1] Gaz. des Hôpitaux, 1861.

ing in the same general sheath close to one another, and ultimately after the disappearance of the old sheath of Schwann they develop into independent fibres. Hence, at a certain time there is the appearance as of several nerve-fibres in a single sheath."

Benecke[1] and Bakowiecki state that the nuclei of the sheath can be seen multiplying, elongating, and forming an axis-cylinder by joining each other in the long axis of the nerve, the medullary substance of the sheath of Schwann being applied around this new cylinder.

Leegaard claims that regeneration starts in the protoplasm within the sheath in the neighborhood of the nuclei, fine grayish threads becoming differentiated in the interannular segments and running together into a continuous fibre.

Gluck describes the union as occurring by means of an elongation of the already multiplied nuclei, the myeline and sheath of Schwann being formed later.

It seems almost certain that from the nuclei of the sheath new axis-cylinders are formed. The oval and spiral-shaped nuclei seem to be identical structures with the nuclei of the sheath. They arrange themselves in bundles parallel with the nerve-trunk. This elongation finally becomes transformed into fibres around which the myeline of the sheath arranges itself. In old cases, when regeneration has not taken place, the nerve-fibres disappear, and are replaced by connective tissue.

Bowlby's conclusions are:

1. That the nuclei of the sheath of Schwann (which are developed from epiblast) form the new axis-cylinders.

2. That the myeline is subsequently formed around the new axis-cylinder.

3. That the peripheral end may become regenerated without forming any union with the proximal extremity, but that it again tends towards degeneration if union fails.

Microscopical Conclusions.—Howell concludes that the degenerative changes and the subsequent regeneration take place as follows:

a. Segmentation of the myeline and axis-cylinder at the intersegmental lines.

b. Proliferation and migration of the internodal nuclei.

c. Secondary fragmentation and absorption of the myeline (and the contained *débris* of the axis) most active in the neighborhood of the nuclei.

d. Increase of protoplasm around the nuclei, forming, finally, a continuous band of protoplasm lying in the old sheath.

e. Formation of a new sheath in the periphery of the band, thus making an "embryonic fibre."

f. Union of the embryonic fibres of the peripheral end with those similarly formed in the central end; the union taking place in the intervening cicatricial tissue.

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[1] Bowlby, Injuries and Diseases of Nerves, 1889, p. 23.

g. Formation of myeline in the peripheral end as isolated drops, usually seen first near the nuclei. These afterwards unite to form a continuous tube. The formation of the myeline proceeds centrifugally, starting from the wound.

h. The outgrowth of new axes from the old axes of the intact fibres of the central end, the outgrowth following quickly upon the development of the myeline.

i. In the central end, especially when connection with the periphery is not made, several new fibres may form within the sheath of an old one to take the place of the portion degenerated. Each of these may develop myeline and receive a branch from the axis-cylinder above.

A careful review of the above experiments and a study of the microscopical appearances as exhibited in the figures clearly demonstrate that—

1. Functional restoration is possible.

2. The closer the apposition the more speedy and complete will be the restoration.

3. Union is accomplished chiefly by the reaching out and development of nerve-fibres from the divided proximal end, these fibres pushing their way across the connecting link of fibrous tissue. The fan-like projection of these fibres is marked in each case.

4. Engrafted nerve-tissue or flaps cut from the nerve may serve as a framework for new tissue, or may produce embryonic nerve-fibres capable of assisting in reunion.