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For many years a method for uniting severed nerves has been used in experiments in my laboratory which has proved so superior to the conventional suture methods that the possibility of adapting it to the surgical needs of human beings deserves serious consideration. While the studies pursued with this method have branched into many phases of the problem of nerve restoration, the following brief account will confine itself to those aspects which seem to be of immediate practical interest.

The method consists in splicing the stumps of a severed nerve by inserting them in a closely fitting sleeve of live artery. First devised for use in the frog and toad [1] the method was then applied to the rat [2] and has lately been used extensively in work on this animal. Save for a brief note,[3] no special description of the technic and of the processes of nerve regeneration following its use has as yet been given. This missing information will be supplied in the present paper.

It should be understood from the outset that the purpose of using an arterial link to reunite ends of a nerve is primarily to provide a firm tie between the stumps of a sort that will favor regeneration of nerve fibers and prevent formation of scar tissue. It is not intended as a means of bridging larger gaps in a nerve by providing regenerating fibers with a pipeline, as it were, for which purpose "tubulation" or "tubularization" of nerve stumps has been used, with varying success, in the past.[4] As nerve ends can never be strictly apposed in the microscopic sense and, in fact, for best histologic results never should be,[5] the function of the arterial tube as a guide for nerve fibers will also come up for consideration, but this is a secondary matter. The main purpose of use of the arterial sheath is to eliminate the need of suturing the stumps together, so that the various hazards to nerve regeneration inherent in ordinary methods of suturing may be avoided. Owing to the greater tensile strength of the arterial link as well as to some other advantages to be discussed in subsequent paragraphs, tube splicing seems to be

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1. Weiss, P.: Selectivity Controlling the Central-Peripheral Relations in the Nervous System, Biol. Rev. **11**:494-531, 1936.

2. (*a*) Sperry, R. W.: The Effect of Crossing Nerves to Antagonistic Muscles in the Hind Limb of the Rat, J. Comp. Neurol. **75**:1-19, 1941; (*b*) Transplantation of Motor Nerves and Muscles in the Forelimb of the Rat, ibid. **76**:283-321, 1942. (*c*) Weiss and Campbell: Unpublished data.

3. Weiss, P.: Re-Union of Stumps of Small Nerves by Tubulation Instead of Suture, Science **93**:67-68, 1941.

4. Stookey, B. P.: Surgical and Mechanical Treatment of Peripheral Nerves, Philadelphia, W. B. Saunders Company, 1922. Pollock, L. J., and Davis, L.: Peripheral Nerve Injuries, New York, Paul B. Hoeber, Inc., 1933.

5. Nageotte, J.: L'organisation de la matière dans ses rapports avec la vie, Paris, F. Alcan, 1922.

superior, on the whole, to the only other sutureless technic of nerve union, the blood plasma technic of Young and Medawar.[6] However, there will be situations in which arterial splicing is not practicable while plasma suture is.

The adequacy of the arterial link has been proved both with regard to its mechanical function of tying and holding the nerve ends together and with regard to its capacity to provide most favorable conditions for the outgrowth of regenerating fibers from the proximal stump and the invasion of the peripheral stump. The main advantages are as follows:

1. Clotting blood plasma and tissue fluid seal the arterial sleeve tightly to the surfaces of the inserted nerve ends. As adhesion is proportional to the size of the adhering surfaces, the tensile strength of an arterial juncture, with the outer wall of the nerve and the inner wall of the artery in extensive contact, is naturally much greater than that of end to end blood plasma fusion, as practiced by Young,[7] just as two threads glued lengthwise to a common third thread are more firmly united than if they were merely joined end to end.

2. The arterial link permits, without loss of holding strength, leaving a slight gap between the nerve ends, which seems to be beneficial to smooth nerve regeneration.

3. The introduction into the nerve of a foreign body, such as catgut, silk or nylon, is avoided. This not only precludes the foreign body reactions common in such cases but, more significantly, eliminates the disorientation effects which suture threads exert on the regenerating nerve fibers in their vicinity.

4. Longitudinal stresses, which would otherwise be taken up by the unelastic suture threads, are transmitted through the tissue matrix filling the gap between the two cut ends and force that matrix into longitudinal orientation, which, in turn, imparts corresponding orientation to the regenerating nerve sprouts.

5. As a corollary of the preceding statement, the disorientation commonly observed in the so-called scar region is prevented, which reduces the incidence of fiber branching and of formation of local neuromas to insignificant proportions.

6. The uninterrupted canalization between the two nerve stumps prevents both the escape of bundles of nerve fibers into the surrounding tissues and the ingrowth of scarifying fibrous tissue into the wound.

7. Branching and diffusion of fibers at the suture level thus being avoided, conditions are more favorable for an orderly point to point reconnection between central cells and peripheral organs than is common in nerve regeneration. This, in turn, must be expected to have important bearings on functional restoration. Instead of allowing fiber branches to scatter widely all over the peripheral stump, the arterial sleeve insures the preservation of some degree of topographic localization throughout the process of regeneration.

8. Arterial splicing makes it possible to mend small nerves for which ordinary suturing would not be feasible.

In support of these statements, I shall present the results of a thorough histologic study of 23 sciatic nerves of rats spliced with arterial segments, 10 of which were studied in regularly spaced cross sections while 13 were studied in serial longitudinal sections. On 8 of the transversally cut nerves complete fiber counts through representative regions, old and regenerated, were made. Moreover, most

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6. Young, J. Z., and Medawar, P. B.: Fibrin Suture of Peripheral Nerves, Lancet **2**:126-128, 1940.

7. Young, J. Z.: The Functional Repair of Nervous Tissue, Physiol. Rev. **22**:318-374, 1942.

animals before being killed were subjected to physiologic tests in which the isometric tension produced by the gastrocnemius muscle on stimulation of the regenerated sciatic nerve was recorded.

TECHNIC

While many kinds and sizes of nerves have been used, the following description will be confined to the suture of the sciatic nerve in rats of between 200 and 300 Gm. body weight. Arteries of proper diameter are furnished by the trunk aortas of smaller animals and the carotid and femoral arteries of larger animals. The artery which appears in all figures 1 *B* to 7 of this report is a segment of aorta.

The sciatic nerve is severed in the proximal part of the thigh, either at the level where it is still uniform or at a more distal level, where it is already internally subdivided into a peroneal and a tibial branch. After transection the two ends of the nerve are inserted into an arterial sleeve previously prepared in the following way. A segment of artery about 1 cm. in length is transferred into Ringer's solution, where it is freed from its blood content by gentle squeezing. A specially designed splicing forceps is then introduced into the empty lumen. The procedure is illustrated in figure 1 *A*. The splicing instrument consists of a forceps terminating in two half-cylinders, which when closed form a tube. Into this fits a solid core of conic shape (fig. 1 *A,a*). For use on smaller nerves the half-cylinders are fashioned by grinding down hypodermic needles of suitable gage. These are then soldered to the prongs of a steel forceps. For greater rigidity the proximal part of the needle is filled with solder. Both halves are so adjusted that when the forceps is closed they will meet edge to edge. Since the base of the conic core has the same diameter as the outside of the tube, the closed forceps and the inserted core form a continuous tapering rod. In this position the instrument is introduced into the artery, as shown in figure 1 *A, b*. From the tapering core the arterial fragment is then pulled over the cylindric end of the closed forceps, whereupon the core is withdrawn and the forceps slightly opened so as to distend the artery (fig. 1 *A, c*). Since in the case of thick-walled arteries the spring of the forceps may not be sufficient to produce distention, it is advisable to fasten a setscrew between the two prongs of the forceps, the turning of which can force the branches apart. The open forceps is then slipped over one of the nerve stumps so that the cut end will come to lie between the two prongs inside the widened orifice of the arterial sleeve. After the nerve end is clutched by closing the forceps, the arterial fragment is pulled back from the forceps over the nerve, as shown in figure 1 *A, d*. When the forceps is withdrawn, about one half of the length of the sleeve is left over the nerve end while the other half is empty (fig. 1 *A, e*).

To introduce the other nerve end into this empty part, an instrument illustrated in figure 1 *A, f* and called the "spreader" is used. It consists of a clip fashioned from an elastic wire band and acting like a forceps with reversed tips. When this clip is closed by lateral pressure with a needle holder, the two free end pieces are brought in apposition and can then be easily inserted into the open end of the artery. On release, the spring of the instrument opens the artery, as shown in figure 1 *A, g*. By appropriate bending of its apex, the elasticity of the instrument can be adjusted so as to distend the artery to just the desired amount. The nerve stump is then introduced into the opening and pushed on until it meets the previously inserted stump. When the spreader is withdrawn, the released artery by its elasticity clamps down on the second nerve stump. The surfaces of the spreader must be polished, for rough edges tend to pull the nerve out again. The grip of the arterial sleeve on the two nerve ends is then tightened by stretching the artery lengthwise with two pairs of forceps. This secondary elongation entails a slight separation of the formerly closely apposed cut surfaces, as is shown in figure 1 *A, h*. However, such a small gap, measuring in length not more than the diameter of the nerve, is not detrimental but apparently even favorable to smooth crossing of the regenerating fibers from the proximal into the peripheral stump.

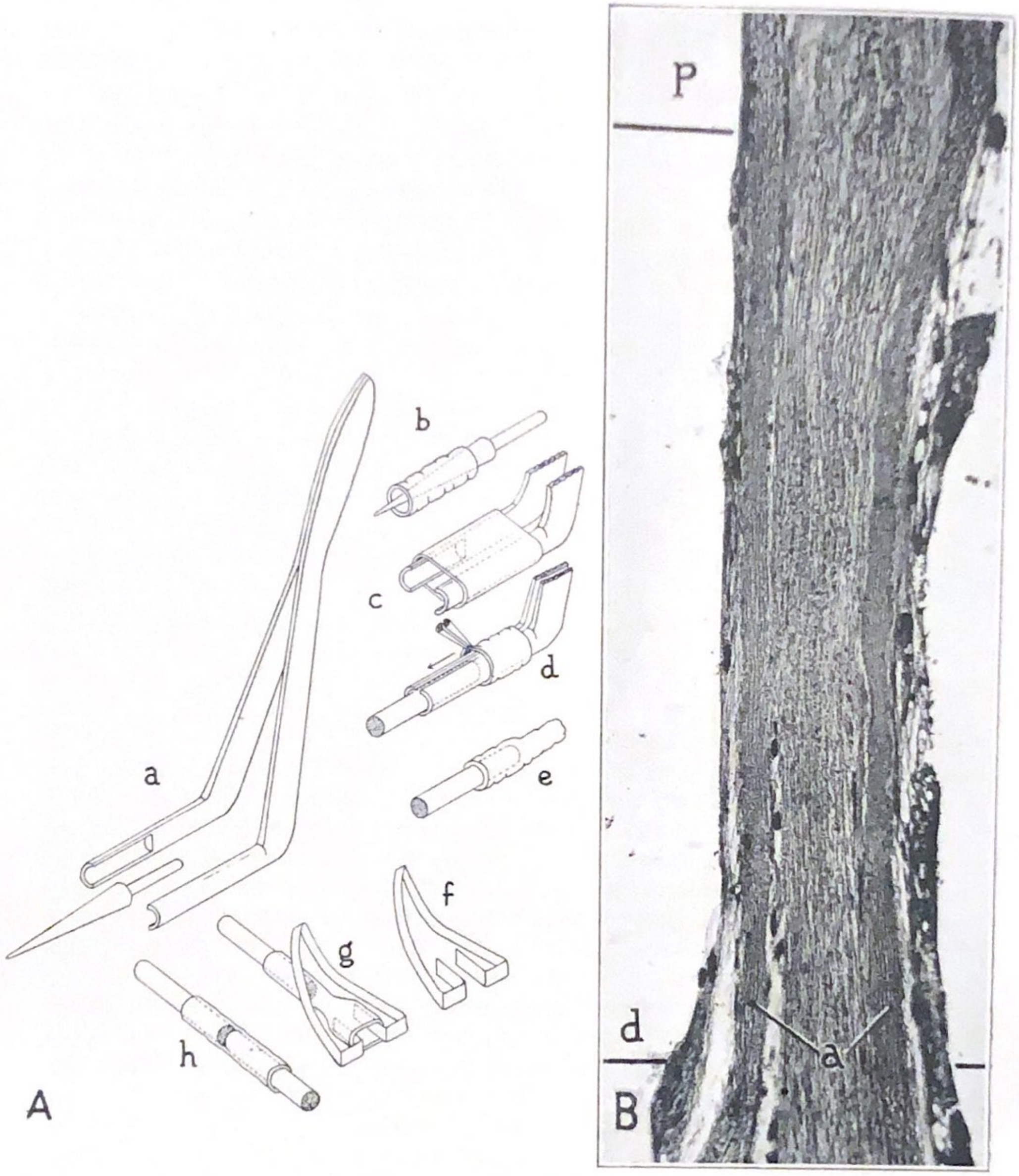

Fig. 1.—*A*, splicing technic. An explanation is given in the text. *B*, longitudinal section through regenerated sciatic nerve spliced with arterial sleeve, at transition from proximal (*p*) to distal (*d*) stump, one hundred and fifty days after operation (× 41). *a*, wall of artery (note lamination).

During the operation the wound bed may be irrigated with Ringer's solution, which prevents the sticking of the instruments to the tissues. The splicing should not be done until intraneural bleeding from the cut section has ceased. In fact, if there should be secondary bleeding into the gap between the two stumps after the splicing, it is indicated to withdraw the peripheral stump from the sleeve again, remove the blood clot and resplice. The effects of plasma clots left between the stumps are being further investigated and will be reported in a later communication.

After the splicing, all excess fluid is blotted or sponged from the surroundings. Leaving the exposed area to dry for several minutes results in a firm tie between the wall of the artery and the inserted nerve stumps. Residues of blood plasma along the inner wall of the artery obviously help in cementing the union. That this is not absolutely essential for successful splicing, however, is demonstrated by the fact that arteries kept in Ringer's solution on ice for one or two days are quite adequate, although their inside is much more slippery than that of fresh artery. When these are used, the clotting of the fresh tissue juice along the sticky surface of the nerve obviously provides the sole cementing agent. The wound may then be closed. Experiments with prolonged exposure show that after fifteen minutes the tie has become firm enough to withstand moderate tension. Pending more exact determinations of the tensile strength of arterial joints at various intervals after the operation, it may be stated that in some test experiments in which the wound was opened a few hours after the operation noticeable pull was required in order to break the link between the two nerve stumps. Since the adhesive power between arterial wall and nerve surface is proportional to the extent of surfaces in contact, and hence to the length of the arterial sleeve, the latter will have to be made the longer the more tension the spliced nerve is expected to sustain.

HISTOLOGIC OBSERVATIONS

A number of typical examples may serve to illustrate the type of nerve regeneration obtained with arterial splicing. Fixation in Bouin's fluid under stretch and impregnation with silver salts according to the method of Bodian, sometimes supplemented by staining with Mallory-azan stain, have been used throughout.

Figure 1 *B* presents a longitudinal section through the region of a splice one hundred and fifty days after the operation. The proximodistal direction is indicated in the picture. The central mass of nerve fibers can be seen to be bounded on either side by the laminated arterial wall. The seven to eight layers of elastic tissue forming this wall can be clearly recognized. The levels of the original cut surfaces can be reconstructed from the extent of the original epineurium of the nerve stumps. Since the perineurium and epineurium have failed to regenerate, their margins indicate approximately the farthest extent of old nerve. These levels are marked in the figure by solid lines. Between them the nerve fiber masses are devoid of epineurium and sheathed directly by the arterial sleeve. This region then corresponds roughly to the former gap. Since there may have been some slight retraction of the epineurium on either side of the gap, the original distance between the nerve ends may not have been quite as large as it would seem from the final picture. At any rate, this is the region which corresponds to the so-called scar region, or suture line, of a nerve sutured by ordinary methods. It can be seen from the picture that in this area the nerve is attenuated. This is due in part to the absence of the epineurium and in some measure to the smaller size of the nerve fibers. As will be shown later, however, it does not express a significant decrease in the number of fibers.

Several striking features of the regenerated nerve become obvious at once. The nerve fibers run in a straight course and in parallel orientation from the proximal stump into the gap region, continue without deflection or confusion through this region and pass on straight into the peripheral stump. Nowhere is there evidence of the profuse branching, straying about and intermingling of fibers commonly observed at the transition from the proximal to the peripheral stump of nerves sutured by ordinary methods.

Figure 2 gives an enlarged view of the transition from the gap region into the peripheral stump of the same nerve as in figure 1 *B*. The entrance into the old peripheral stump is marked by the appearance on one side of the picture of the old epineurium; on the other side some fat tissue has penetrated. The central part of the picture is taken up by the strands of regenerated nerve fibers. These form a compact mass, packed about as densely as they are in normal nerve. They

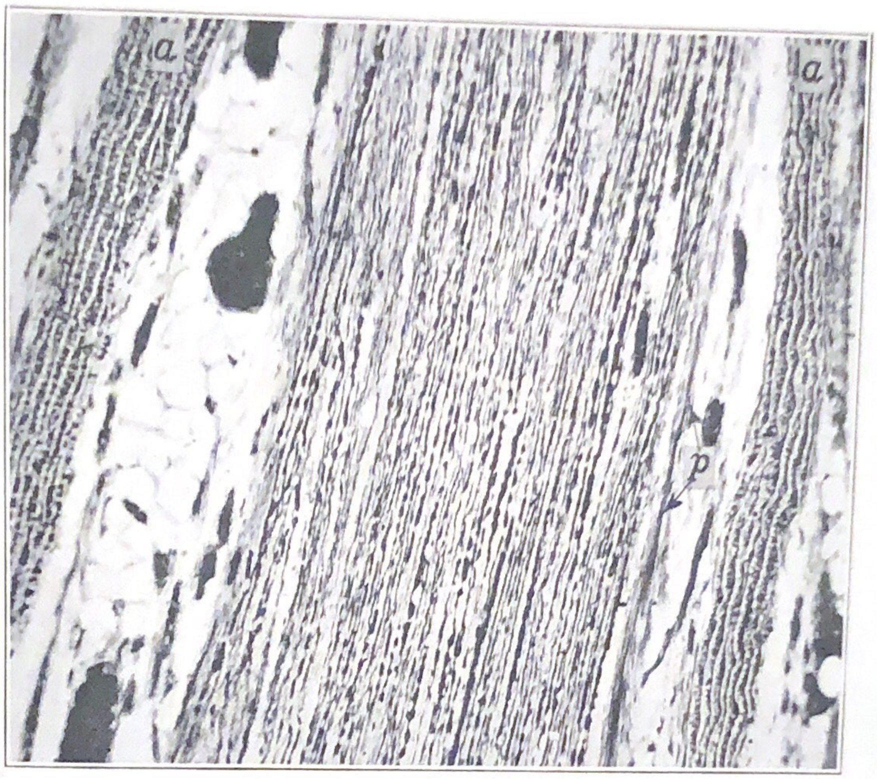

Fig. 2.—Same preparation as in figure 1 *B* at transition from "gap" to peripheral stump (× 115); *a*, arterial wall; *p*, perineurium.

follow a well oriented straight course. Their size varies from very thin to relatively large fibers. In estimating size of fibers it must be remembered that with the methods of fixation and impregnation used in these studies large axis-cylinders collapse in many places along their course, which gives them the appearance of a string of beads, each myelin segment showing several constrictions. A further discussion of size of fibers will be presented later.

To either side of the nerve mass one sees spaces filled partly with vascularized fat tissue and partly with loose connective tissue, the extent of the latter being exaggerated by shrinkage during fixation. These layers separate the nerve core from the wall of the artery, which can be recognized by the characteristic lamination of the elastic tissue. Lack of intimate contact between the nerve fibers and the inner wall of the artery is a frequent occurrence near the original arterial openings, where the epineurium and adhering loose connective tissue were tucked into the artery. In many spliced nerves, of which the present one is a typical example, there has been a definite tendency of this tissue to become converted into fat tissue, which then has remained interposed between the arterial wall and the surface of the nerve. Whether the breakdown of myelin with the liberation of phospholipids in this region has anything to do with this transformation into fatty tissue remains a matter for speculation. At any rate, this process remains localized about the ends of the sleeve, while in the intermediate zone close contact between the nerve fibers and their arterial container is preserved. This is further illustrated by the study of cross sections.

Figure 3 shows cross sections through a spliced and regenerated sciatic nerve one hundred and eighty-one days after operation at five different levels. The location of these levels is indicated in the accompanying diagram (fig. 3 *F*). The nerve had been transected at a level distal to its bifurcation into the tibial and peroneal divisions. Section *A*, through the proximal stump near the proximal end of the arterial sleeve, shows the two nerves with their perineuriums, surrounded by the artery. Some fat tissue can be seen wedged between the old epineurium and the arterial wall. This level is still more than 2 mm. proximal to the original level of transection. Yet the tibial nerve (lower left) gives evidence of being composed largely of regenerated fibers. In contrast, the peroneal division (upper right) shows essentially the organization of normal nerve, although it, too, contains a certain contingent of regenerated fibers. The situation is explained by the fact that ascending traumatic degeneration following transection of a nerve may extend several millimeters centrad from the wound, so that regeneration actually starts from a level slightly proximal to the actual level of sectioning. The difference between the peroneal and the tibial nerves in this case is simply due to the fact that after transection the latter has retracted a little farther in its sheath (fig. 3 *F*). Section *B*, which lies 2.5 mm. distal to *A*, shows the end of the proximal stump of the peroneal nerve, while the fibers of the tibial nerve at this level have already entered the gap between the original stumps. Consequently, the peroneal nerve (in the center) is still surrounded by some of its perineurium, while the fiber masses emerging from the tibial nerve (on the left) are applied directly to the inner wall of the artery. Section *C*, which is 2 mm. distal to section *B*, lies entirely within the gap region, and here the fiber bundles fill the lumen of the artery completely, except for a small extension of vascularized fat tissue on the right.

This is, then, the aspect in cross section of the fiber masses between their emergence from the original proximal stump and their entrance into the original distal stump; in other words, the suture line corresponding to the scar region of ordinary nerve sutures. The fibers can be seen arranged in small bundles, typical of regenerated nerve, with some larger spaces in between. It will be noted that nearly all fibers appear hit in their cross section and that practically none course in the plane of sectioning. This is merely another expression of the straight, parallel, longitudinal orientation of the regenerated fibers. Section *D*, 2.5 mm. distal to *C*, is from the region of the old peripheral stump of the tibial and peroneal nerves, still inside the arterial sleeve. Both nerves are completely refilled with nerve fibers, surrounded by their old perineurium and again accompanied by fat tissue, as previously discussed. Section *E* introduces a still farther distal level, 10 mm. from *D*, where each nerve has become subdivided into branches. Except for a few blank spaces, these branches have received their full complement of nerve fibers, and, as can be seen, many of these fibers have assumed fairly large diameters.

Figure 4, finally, gives details at higher magnification from sections 3 *A*, *C* and *D*, respectively. Except for an occasional straggler coursing obliquely or transversally, the vast majority of fibers can be seen to be oriented perpendicular to

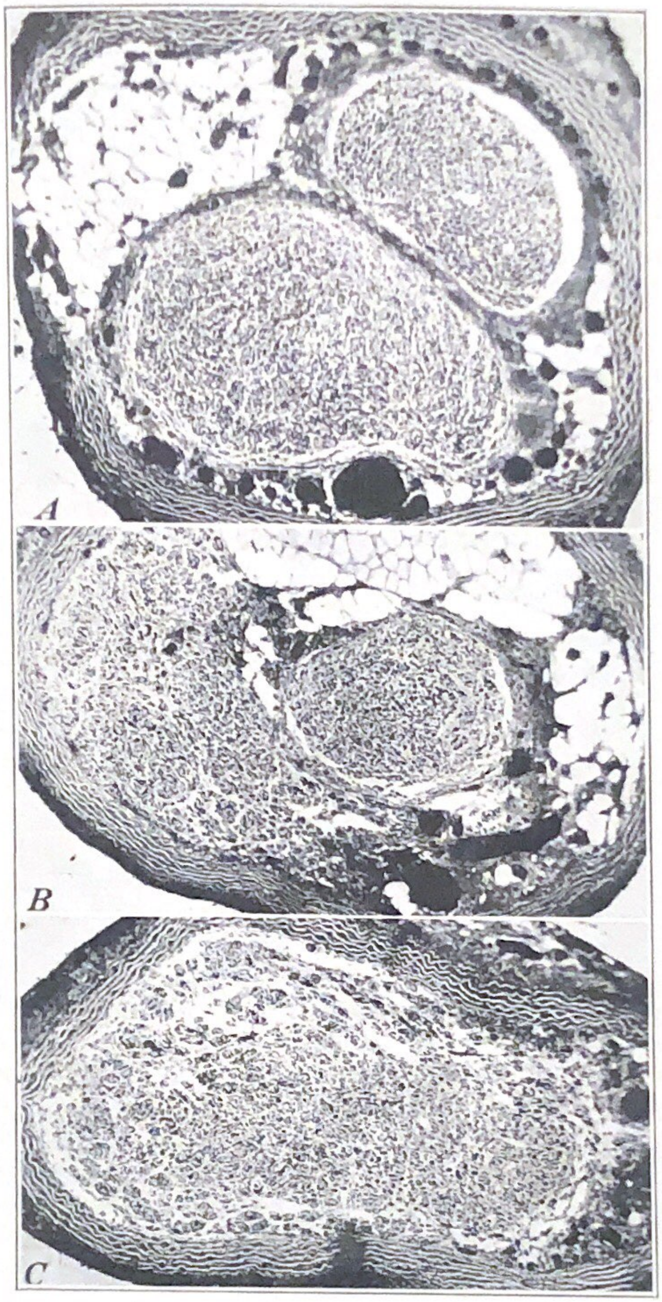

Fig. 3.—Cross sections through an artery-spliced and regenerated sciatic nerve one hundred and eighty-one days after the operation. Further explanation is found in the text (× 62).

the plane of sectioning, i. e., parallel to the axis of the nerve. A comparison of the middle section, which runs through the gap region of the nerve splice, with the other two sections reveals that on the whole the reorganization of the nerve is somewhat further advanced inside the old stumps, both central and peripheral, than it is in the intervening zone. In the latter the fibers are more loosely packed, there is a somewhat greater proportion of endoneural tissue and there seem to be fewer fibers of the largest caliber. It would seem, therefore, that in the peripheral stump, where the fibers had the benefit of traveling inside the old

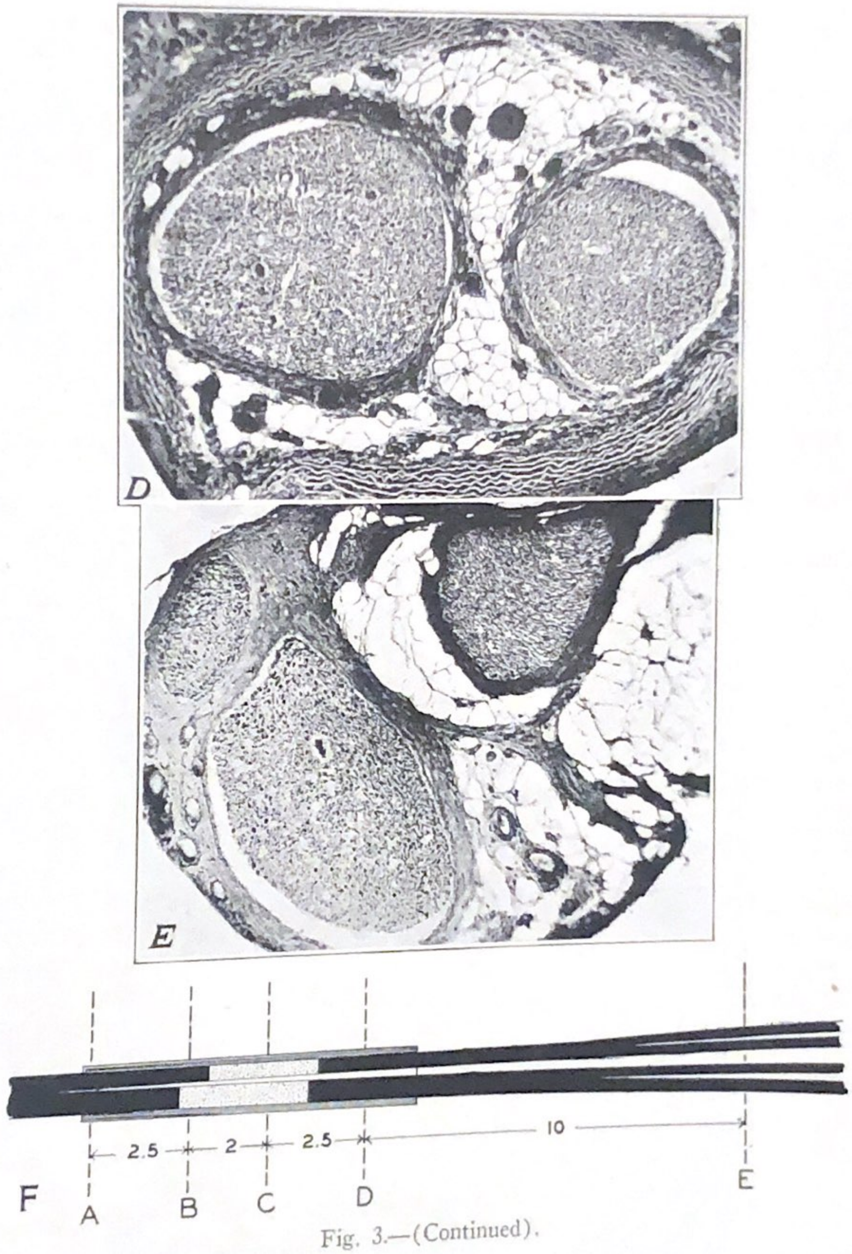

Fig. 3.—(Continued).

degenerated Schwann sheaths, reorganization and maturation took place at a slightly faster rate than in the pathless area of the gap. Sections from other spliced nerves confirm this impression. However, it will require more intimate studies to determine whether the observed differences are significant.

With regard to size of fibers, a striking difference exists between the old fibers in the proximal stump and their regenerated peripheral parts, as seen in figure 3 *B* and *C*. The left upper half of figure 3 *A* shows a sector of the original fiber complement of the peroneal nerve. While many of these fibers were hit slightly obliquely and therefore appear somewhat larger, most of them, particularly toward

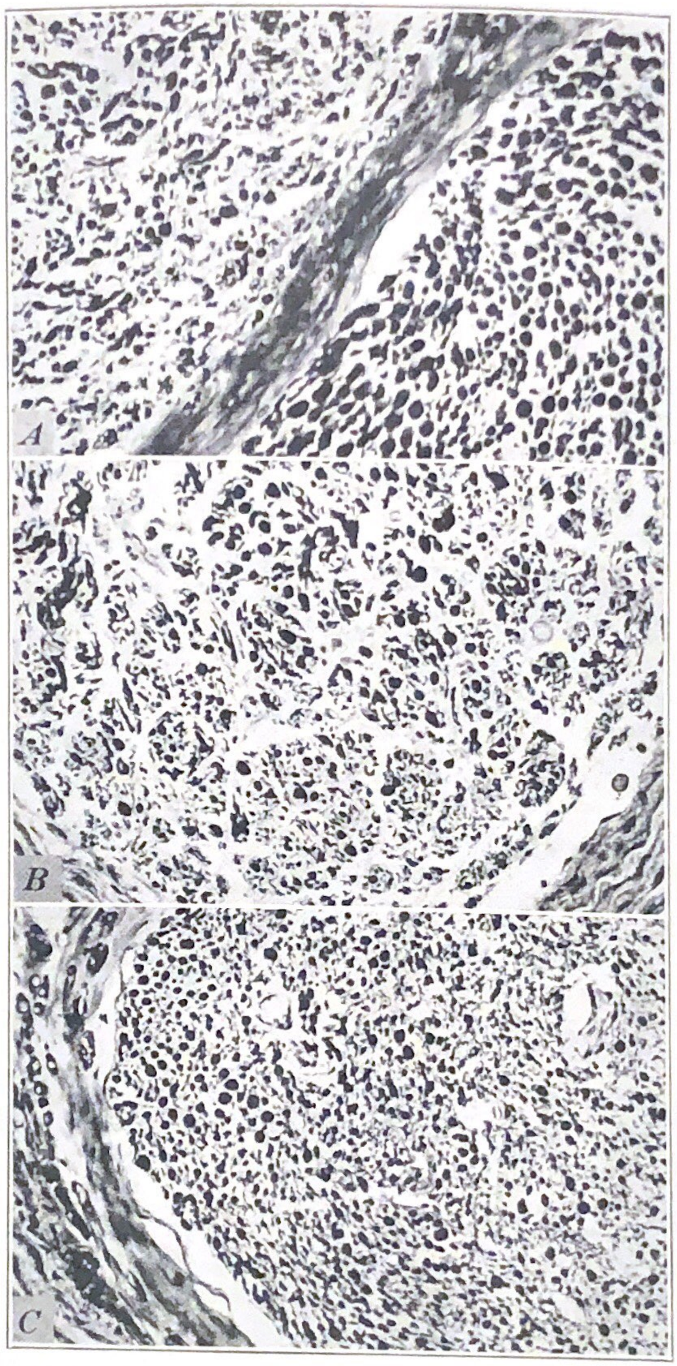

Fig. 4.—Details from cross sections *A*, *C* and *D* of figure 4 (× 210).

the center of the nerve, appear in straight cross section. As one can readily see, the proportion of large diameter fibers in this old nerve is much greater than is to be found at any one of the more distal levels. It is well known that the newly regenerated branches, growing out from a severed central stump, are all very thin fibers of more or less equal diameter. It is only secondarily that the peripheral parts of some of the regenerated fibers will grow in thickness, tending toward the restoration of the differentials of fiber size existing in normal nerves. How closely the original pattern of size distribution is restored and to what extent the resumption of a definite caliber is controlled by the origin of the fiber branch, the path it has taken, the length it has attained and the termination it has reached have not yet been systematically investigated, although some occasional attention has been given to the problem. However this may be, it is obvious that in the present nerve the fiber composition of the peripheral trunk has not yet been fully restored to its original condition in six months after the transection. By far too many fibers are still in the small and very small classes, with fibers of the larger caliber comparatively scarce.

All other nerves studied on which the operation was performed properly conform to the type of regeneration just described. In all of them the nerve fibers have retained their straight longitudinal course throughout the gap and peripheral stump. Occasionally single fibers or small bundles do run off at an angle for short distances, but these occurrences seem to be negligible when contrasted with the strict longitudinal orientation of the bulk of the fibers. Perineurium and epineurium have not regenerated, and within the stretch intervening between the original cut levels the fibers are in direct contact with the inner surface of the arterial sleeve, which within this area, then, serves as nerve sheath.

The vascular supply of the regenerated nerves is partly intraneural, with most vessels running lengthwise inside the nerve, and partly perineural, with accessory vessels from the interstitial fat tissue entering the nerve.

FIBER COUNTS

Counts were made of the number of nerve fibers seen in cross sections of 8 of the nerves operated on.[8] Data for 5 of these, for which complete counts are available through all three critical levels, i. e., through proximal stump, gap and distal stump, are included in the following tabulation. The remaining 3 counts are incomplete in that no enumeration was made at the level of the gap, and these are therefore omitted.

The counts were made according to the method regularly used in this laboratory in the past.[9] The margin of error of this method was found in earlier observations to lie below 2 per cent for fibers stained for myelin [10] and within 6 per cent for silver-impregnated fibers.[9] In view of the large number of very fine fibers present in newly regenerated nerve, increasing the difficulty of identification, the counting error may be considered higher in the present tabulations. The results are summarized in the table.

The most striking point is the close correspondence between the number of fiber sections counted in the old proximal stump of the sciatic nerve and the number of regenerated fiber sections within the gap area. Only in nerve *B* does the gap show a deficit of nearly 20 per cent, and this is readily explained by the fact that in this experiment the artery had in one place sustained a break, through which

8. The author is indebted to Dr. Raymond Litwiller for assistance in the making of fiber counts.

9. Litwiller, R.: Quantitative Studies on Nerve Regeneration in Amphibia: I. Factors Controlling Nerve Regeneration in Adult Limbs, J. Comp. Neurol. **69**:427-447, 1938.

10. Weiss, P.: Further Experimental Investigations on the Phenomenon of Homologous Response in Transplanted Amphibian Limbs: II. Nerve Regeneration and the Innervation of the Transplanted Limbs, J. Comp. Neurol. **66**:481-535, 1937.

a mass of fibers escaped into the surroundings so as to be lost for the count. In all other instances the difference between the two levels lies within the limits of the error inherent in the method. These figures, therefore, bear out completely the evidence of the histologic observations, according to which, on the whole, each fiber of the proximal stump has during its regenerative outgrowth remained single, without bifurcation. The fiber counts inside the distal stump show a distinct drop below those of the gap, varying with the distance at which the count was taken. This drop can be accounted for by the branching off from the main nerve trunks of some small fiber bundles which were omitted in the distal counts. That the decline is not necessarily an expression of incomplete regeneration is demonstrated by the fact that even in the youngest splice (*A*), studied seventy-four days after the operation, the distal stump has become fully repleted.

FUNCTIONAL OBSERVATIONS

While the relation between morphologic regeneration and functional recovery will be more fully discussed in a subsequent paper, a few remarks on the subject seem in place. Obviously the stage has been passed when one can acquiesce in

Results of Fiber Counts

Nerve	Days After Operation	Number of Fibers			Length of Gap, Mm.
		Proximal Stump	"Gap"	Distal Stump	
A	74	5,415	5,240	5,210	3.5
B	137	5,235	4,245*	3,218	4.5
C	143	4,435	4,855	4,075	Undetermined
D	153	4,613	4,770	3,425	2.0
E	172	5,590	5,545	4,095	Undetermined

* Break in arterial wall with extensive escape of fibers.

such general statements as that function has become "improved" or "partially restored" or has remained "abnormal." Neither sensory nor motor functions are in themselves entities; they are complex phenomena in which each phase is differentially affected by denervation and nerve regeneration. For each phase definite criteria must be established, and functional restoration must then be described in terms of these criteria. On the motor side restoration of trophic influences, electric excitability, transmissibility at the myoneural junction, reflex action, muscular power and, finally, coordination must be given separate consideration in relation to nerve regeneration. As for the restoration of muscle power, an adequate test consists of determining the maximum tension which the reinnervated muscle can produce on direct stimulation as well as on indirect stimulation through its nerve. Registered isometrically, the tension developed after direct stimulation of the muscle is a measure of the amount of functionally adequate contractile tissue, while isometric tension developed in the muscle after electric stimulation of its nerve with supramaximal shocks gives a measure of the fraction of total contractile tissue which has become reinnervated.

In the experiments with the best results, the maximal tension obtained from a gastrocnemius muscle reinnervated from a spliced sciatic nerve was approximately equal to that recorded from the opposite gastrocnemius muscle, with undisturbed innervation.[11] This means that the muscle on the side operated on either had suffered only a minor denervation atrophy or else had become restored to its original size after reinnervation. In such instances, tensions developed after supramaximal stimulation of the nerves were likewise nearly symmetric on the two sides, proving that all of the muscle fibers in contractile condition had received reinnervation. This condition was found as early as ten weeks after splicing. This is remarkable, inasmuch as histologic preparations of these nerves reveal that most of the regenerated fibers are still rather immature, i. e., of small diameter with myelination in its early stages. In other words, the power developed by a motor unit does not depend on the state, size and degree of maturity of the efferent neuron provided neuromuscular transmission is established at all. This, of course, merely expresses the all or none nature of the contraction of muscle elements activated by nerve excitation.

In several instances, however, in which the histologic picture of the sciatic nerve as well as the fiber counts proved that the neurotization of the peripheral stump was fairly complete, the muscle power on the side of the operation, nevertheless, remained definitely deficient. Inasmuch as in most of these instances a comparison of tensions developed after direct and indirect stimulation showed that no major part of the muscle had failed to receive innervation, the weakness must be ascribed to permanent atrophy rather than to incomplete reinnervation. Such atrophy is usually evident to gross inspection, and quantitative determinations have not as yet been made. In the case of nerve B of the table, for instance, in which in spite of a sizable escape of fibers, a good two thirds of the original fiber complement of the proximal sciatic stump was found present in the distal branches at the knee, the gastrocnemius muscle was able to produce only between 10 and 20 per cent of the tension of the opposite, normal, muscle. Why the atrophy goes further in some instances than in others has not yet been determined. It is obvious that the atrophic condition of the muscles does not reflect on the number of fibers regenerated inside of the nerve stump but merely limits the number of terminal branches that will be produced inside the muscle. It is the average size, rather than the average number, of motor units that is reduced in such cases.

Return of muscle power was not paralleled, however, by return of coordinated function. While the return of sensitivity progressed gradually, as evidenced by the increasing reactions of the animals to nociceptive stimuli, motility of the legs remained inadequate. Motor responses consisted of generalized contractions of the several muscles of the leg, rather than of coordinated movements with muscles in orderly well timed operation. In general, the limbs after reinnervation behaved much as those described by Sperry[2a] after crossing peroneal and tibial nerves. Reciprocal contraction of antagonists is absent, and most responses are characterized by the prevalence of rigid plantar flexion. Sperry ascribed this incoordination to the fact that not all muscles innervated by either the peroneal or the tibial division normally operate in phase. Therefore, random redistribution of the nerve fibers of both nerves during regeneration must result in simultaneous contraction of muscles which originally were engaged independently. Since the rat is definitely incapable of any reeducation of its motor apparatus which might serve

11. The use of the side not operated on as control is somewhat objectionable, since Tamaki (Tamaki, K.: Further Studies on the Effect of Section of One Peroneal Nerve of the Albino Rat on the Intact Nerve of the Opposite Side, J. Comp. Neurol. **64**:437, 1936) has shown that unilateral transection of the peroneal nerve in the rat depresses the growth of the peroneal nerve of the opposite intact side. Allowance must therefore be made for the fact that the "control" nerve is itself slightly reduced. Whether the muscle suffers correspondingly has never been determined.

to correct inadequacies produced by nerve crossing or other irregularities of the peripheral nerve distribution,[3a, b] no improvement in the incoordinated condition of the motor responses was to be expected.

A similar explanation may be advanced for the lack of coordination in the present experiments, assuming that a large proportion of the regenerated nerve fibers have come to terminate on muscles other than the ones with which they had originally been connected. This disarrangement of central-peripheral connections was not precluded by the fact that, as one can see from the histologic studies, the regenerating fibers have essentially retained their mutual topographic relations while traversing the scar and passing on into the peripheral stump. For any degree of rotation of the peripheral stump in regard to the proximal stump in the act of splicing must have produced a corresponding distortion of the pattern of peripheral nerve distribution relative to the original pattern and thereby entailed the functional confusion of which the observed incoordinated activity was an expression. In man, in whom the well marked fascicular topography of the nerve furnishes better landmarks for the orientation of the stumps than is available in the nonfasciculated nerves of the rat, a more congruous opposition of nerve sections, such as was advocated, for instance, by Stoffel (Vulpius and Stoffel[12]), would be easier to achieve. It should be remembered, however, that many neurosurgeons do not believe such careful matching of the nerve surfaces to be necessary and that actually in man reeducation, in the sense of a reorganization of the central impulse patterns, might remedy the inadequacies resulting from altered peripheral connections, for which the rat, as has already been stated, has no remedy.

FAILURES

While the arterial splice when properly performed creates the most favorable conditions for smooth and unimpeded nerve regeneration, improper handling of the method may lead to failures just as severe as though no union of the stumps had been attempted. It has been well known since the work of Cajal[13] that even when the stumps of a severed nerve are left separated a trickle of nerve fibers from the proximal stump will finally find its way into the peripheral stump. The mechanism of this reunion, originally postulated to be chemotropic, was suggested by Dustin[14] to be haptotropic, and recent experiments[15] have furnished evidence that it is really a matter of contact guidance, rather than of attraction over a distance. Those nerve fibers which happen to strike on a peripheral degenerated nerve tube of modified Schwann cells form an adhesive surface for other nerve fibers growing out later, so that gradually an oriented path between the proximal and the peripheral stump is established. However, since the pioneering fibers have to traverse the relatively dense connective tissue of the scar and since this tissue does not seem to offer particularly favorable conditions for their growth, regeneration under those conditions remains always quantitatively inferior.

Exactly the same situation prevails when one of the stumps of a spliced nerve escapes from the sleeve. The sleeve, if it does not collapse entirely, becomes

12. Vulpius, O., and Stoffel, A.: Orthopädische Operationslehre, ed. 3, Stuttgart, F. Enke, 1924.

13. Ramón y Cajal, S.: Studien über Nervenregeneration, Leipzig, 1908.

14. Dustin, A. P.: Le rôle des tropismes et de l'odogénèse dans la régénération du système nerveux, Arch. de biol. **25**:269, 1910.

15. Weiss, P.: (*a*) Nerve Patterns: The Mechanics of Nerve Growth, Growth (supp.) **5**:163-203, 1941; (*b*) In Vitro Experiments on the Factors Determining the Course of the Outgrowing Nerve Fiber, J. Exper. Zool. **68**:393-448, 1934.

invaded by fibrous connective tissue no more advantageous for regenerating nerve fibers than ordinary scar tissue. Similarly, any break in the wall of the artery in the region of the splice impairs regeneration in a double way. In the first place, it permits the escape of fibers into the surroundings and, secondly, it opens the interior to the ingrowth of connective tissue from the vicinity of the nerve, which, in turn, leads to progressive fibrosis and strangling of the nerve fibers inside. A break in the arterial wall may be due to accidental injury during the operation or to later erosion of the wall as a result of infectious or autolytic processes. An example of each of these types is presented in figures 5 and 6.

Figure 5 shows the effect of a stab wound in the arterial wall made at the time of the operation. Owing to the lack of regenerative capacity of the artery this wound has remained open and has seriously affected the regenerative

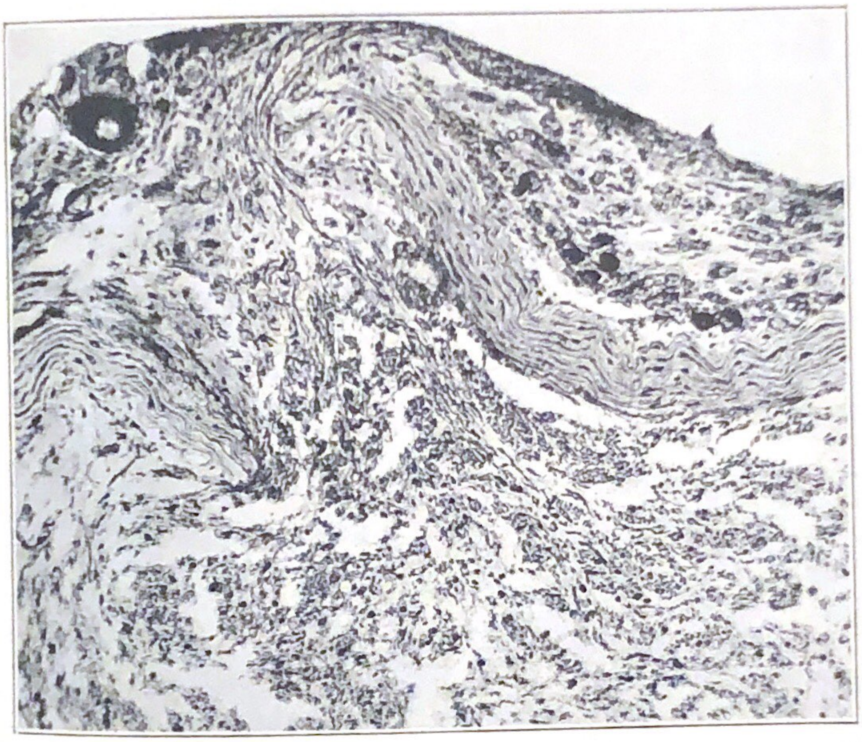

Fig. 5.—Effect of a leak in the arterial wall on regeneration of nerve fibers, thirty-eight days after operation. An explanation is found in the text (× 82).

processs of that area. Not only have the superficial fibers coming up along the perforated side of the wall escaped, but even deeper fiber masses have been deflected toward the leak. The picture one obtains in these cases resembles that of a streaming liquid escaping through a hole in the wall of a tube. Just as in the latter case eddies form—in the vicinity of the leak, so in the case of the nerve an extensive area of disturbance is set up within a certain radius of the opening, and in this area the nerve fibers leave their longitudinal course and converge on the hole. The mechanics of this disruption of the nerve pattern are apparently as follows: Blood plasma and lymph seeping through the hole after the operation coagulate in the direction of the flow and thereby establish a pathway into which the regenerating fibers may turn when they arrive at this level. Ingrowth of connective tissue from the outside along this same pathway, moreover, produces a lateral adhesion, the tension of which further accentuates the local disorientation. Since nerve fibers have been demonstrated to follow such oriented pathways,[15h] a permanent outlet for part of the regenerating fibers is thus established.

Aside from distracting nerve fibers from their straight course, perforations are harmful in that they permit the invasion of fibrous tissue, which eventually establishes sclerotic islands inside the nerve. These, in turn, tend to choke nerve regeneration. While more detailed studies on the subject would be desirable, even our casual observations to date leave no doubt but that nerve fibers which lie embedded in this fibrous tissue remain very thin and immature. Even well oriented fibrous tissue is less pervious to nerve fibers than either degenerated nerve or the exudate of purely neural origin which fills the gap between the two stumps inside a well sealing arterial tube. Besides being a poor growth medium for nerve fibers, fibrous tissue may also be detrimental to the later functioning of nerve fibers contained in it, in that its progressive condensation may set up a pressure block interfering with conductivity.

In a good splice it is evidently the uninterrupted elastic layers that render the arterial wall escape-proof for nerve fibers. While in most experiments the arterial sleeves have retained their original texture throughout their length, a few have been observed in which circumscribed parts of the arterial wall had undergone more or less extensive dissolution. This may assume the aspect of either a local erosion from the outside or a gradual loosening up and swelling of the layers of the wall, with cells from the surroundings penetrating into the spongy mass. Whether these lesions are due to abrasions suffered in the operation or to infection cannot be said. At any rate, within these regions the arterial wall becomes porous, and as a result the pattern of nerve regeneration in such a region becomes thoroughly confused. Evidently, the porous condition of the wall, with the resulting transudation of tissue fluids and the release of longitudinal stress, causes again a widespread disorganization of the matrix inside the arterial lumen, within which the new nerve sprouts grow out, and this entails a complete disorientation of the nerve fibers in that vicinity.

Figure 6 *A* shows a tangential section in the longitudinal direction of the nerve through one such area. The middle portion of the picture shows criss-crossing nerve fibers, many growing transversally and leaving the lumen of the artery by penetrating through the wall. To either side of the artery one can see a dense neuroma consisting of contorted nerve fibers from the escaped masses. In contrast to the effects of large holes discussed in the preceding paragraph, this porosity of the arterial wall, while permitting profuse dissipation of nerve fibers into the surroundings, does not seem to favor reciprocal inflow of fibrous tissue. Consequently, masses of nerve fibers which lie outside the immediately affected area, particularly those deeper in the interior of the nerve, regenerate as well as they otherwise do in intact arterial sleeves. This is illustrated in figure 6 *B*. This figure shows a longitudinal section through the same nerve as figure 6 *A*, slightly distal to the level of the former, traveling through the gap within the intact part of the artery. Here the fibers have remained confined within the tube and have regenerated in strictly parallel longitudinal orientation with no branching or confusion.

The great number of nerve fibers seen in and around an area of decomposition of the sleeve (fig. 6 *A*) offers no correct gage of the actual loss of fibers as sources for refilling of the peripheral stump, for, firstly, their contorted course in this area makes the same fibers appear several times in the same section, and, secondly, there is evidence of extensive branching, attributable to the wealth of obstructions to fiber growth in this region. Accordingly, the peripheral stumps of nerves with lateral eruption of fibers are not as badly depleted after regenera-

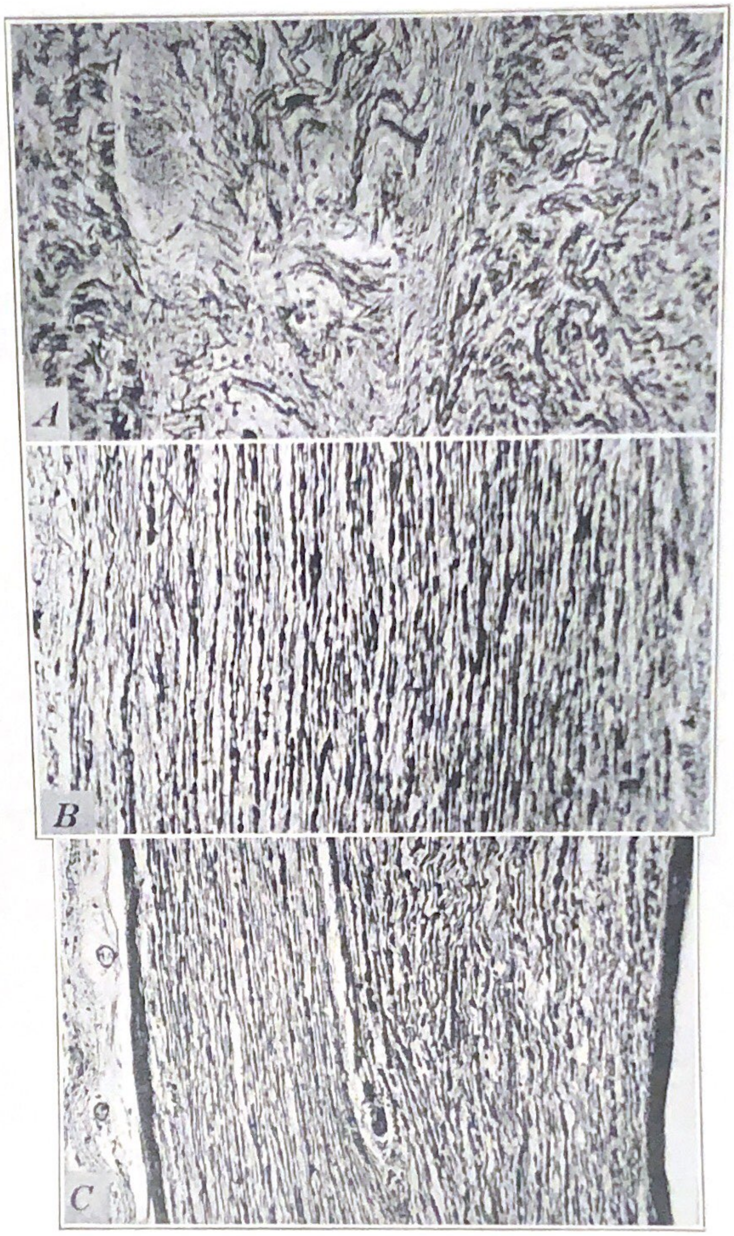

Fig. 6.—Effect of a local lesion in the arterial wall on growth of nerve fibers, one hundred and seventy days after operation. An explanation is found in the text (× 112).

tion as the size of these local neuromas would suggest. Figure 6 *C* shows a longitudinal section through the branching point between the peroneal and the tibial nerve (as in fig. 6 *A* and *B*). It shows the whole tract of the nerve filled with regenerated fibers, and, while the total volume is slightly less than normal, it is not reduced nearly as much as one would have expected if the proximal fiber source had suffered a permanent reduction of such magnitude as figure 6 *B* would seem to indicate. Nevertheless, fiber counts on cross sections demonstrate that leaks in the artery wall do result in a certain permanent deficit of regenerated fibers in the peripheral stump. In one example, for instance, in which during the operation a lateral hole was made in the artery through which fibers later escaped, a fiber count proximal to the break of approximately 6,000 fibers dropped to approximately 2,200 fibers inside the nerve gap beyond the break, which figure rose only slightly farther distally to less than 2,600 fibers in the peripheral branches. Thus, while a negligible amount of regulative branching may have taken place, a definite deficit has remained.

Another type of failure results when a splice is made with arteries too small in diameter to accommodate the nerve without constriction. During the operation such arteries can, of course, be widened to the point where they can be forced over

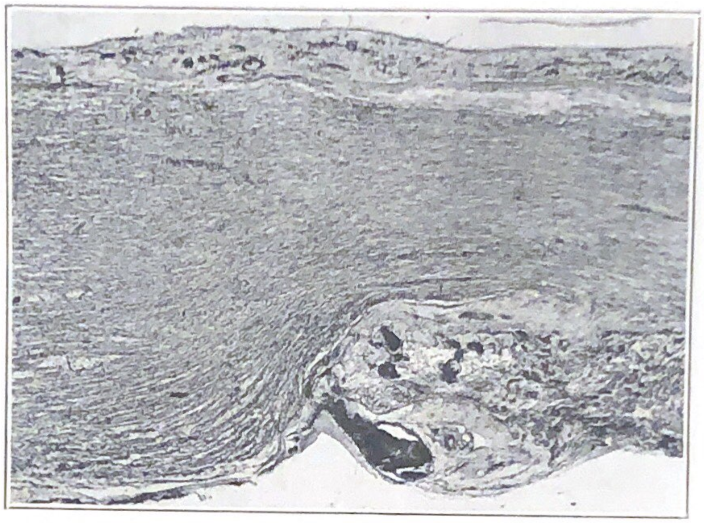

Fig. 7.—Compression of nerve fibers due to constriction of the sleeve; bottleneck at entry of the proximal stump into the sleeve, thirty-eight days after operation (× 56).

the nerve ends, but in postoperative stages they contract again and strangle the nerve in the interior. When this happens, the effects on the nerve are serious. The histologic appearance of such a regenerate is exemplified in figure 7, showing the proximal end of a constricted arterial sleeve. As one can readily see, the sleeve forms a bottleneck, inside of which the nerve fibers are condensed into a tightly packed bundle. Moreover, the proximal stump of the nerve is for some distance proximal to its entrance into the sleeve pathologic in appearance. A conspicuous edema is formed here, which gives the nerve a bulbous shape. The inside of the nerve is loosened up, fibers and fiber bundles are widely separated and retrograde degeneration has proceeded farther centrally than is found after mere nerve section. The edema proximal to the constriction is of great interest. It clearly demonstrates that there is normally in the nerve a centrifugal flow of "lymph." Obstructed by the tight packing of the fibers in the sleeve, this flow is arrested and the dammed-up fluid distends the nerve. A similar observation, namely, an edematous condition of the nerve stump in constricted human nerves, has been reported by Dustin.[16]

Close inspection of the nerve fibers passing through the bottleneck reveals an abrupt change of their size and condition at the level of constriction. Proximal to this level there are many large fibers in advanced stages of maturation, while within the constricted area all fibers are small and immature, like those of very young regenerates. This does not mean that the large fibers have grown only as far as the level of the constriction and there become arrested, but rather that one and the same fiber has assumed large diameter in the proximal part but remained small and undeveloped within the compressed area. This could be ascribed to a sort of inanition effect resulting from the lymph stasis mentioned before, but it is more likely due to the obstruction of the centrifugal flow in the axis-cylinders themselves of some essential factor produced by the nerve cell body and required for continued growth in width of the peripheral fiber. This is suggested by the fact that the fibers just proximal to the level of constriction are often swollen and club shaped, as if some substance passing down the axon had become dammed up on the inside.[17]

The few such constrictions observed thus far were studied only five to six weeks after the operation. Therefore, it is impossible as yet to say whether the immaturity and small size of regenerated fibers under lateral compression are a permanent feature. However, in view of the tight packing of the fibers and the apparently firm stranglehold of the artery, it may be considered doubtful whether these fibers will ever have an opportunity of acquiring larger caliber. Some of these compressed nerves have been studied oscillographically and will be discussed on a later occasion. It may suffice here to say that this condition seems to set up a definite pressure block interfering with conduction along those fibers. Therefore, although complete neurotization of the peripheral stump may be obtained even under these conditions, the functional results of such regeneration are rather inadequate.

It is evident, then, that most failures of the arterial splice are due to improper manipulation during the operation or to the selection of arteries which are either too big, and thus admit extraneous fibrous tissue, or too small, and thus choke the nerve.

COMMENT

Properly executed, the arterial splice leads to a satisfactory reunion between proximal and peripheral stump and creates most favorable conditions for subsequent nerve regeneration, provided the two cut surfaces can be brought within fair proximity. It can be applied wherever there is enough slack on the nerve to permit apposition of the cut surfaces. However, intimate contact between the two ends is neither necessary nor desirable. Pressing the two ends together so as to produce flanging forces the nerve fibers into a tangle which a good suture tends to avoid. Moreover, it must be borne in mind that regeneration of the fibers does not actually start from the level of apposition but begins slightly more proximally, since a variable and uncontrollable amount of retrograde degeneration is bound to precede the onset of regeneration.

It has already been pointed out by Nageotte [5] that a slight gap between the nerve stumps is advantageous for regeneration, and the same general conclusion

16. Dustin, A. P.: Les lésions posttraumatiques des nerfs: contribution à l'histopathologie du système nerveux périphérique chez l'homme. Ambulance de "l'Ocean," 1917, vol. 1, pt. 2, pp. 71-161.

17. Parker, G. H.: On the Trophic Impulse So-Called: Its Rate and Nature, Am. Naturalist **66**:147-158, 1932.

must be drawn from the present experiments. The size of the gap in our experiments can be reconstructed from longitudinal sections as the distance between the margins of the proximal and the distal epineurium. The epineurium, at least under the conditions of our experiments, has shown little tendency to regenerate, and its edges, therefore, mark the limits of the old nerve stumps rather distinctly. If these landmarks are used and allowance is made for the fact that they may have been slightly retracted during the healing process, it becomes evident that a gap up to 3 mm. between the original nerve ends is compatible with good nerve regeneration. Through such a gap regeneration takes place with the same strict orientation, fiber alinement and ease as if the fibers were proceeding inside a degenerated peripheral stump. Larger gaps have not been found equally passable, primarily for the reason that the arteries in such regions, lacking a solid core, tend to collapse so that their lumen becomes partly obstructed.

The question now arises as to what forms the matrix, i. e., the medium in which the nerve fibers grow while traversing the gap. Obviously the gap is no void but is filled with substance even before the regenerating nerve fibers arrive, and the composition and properties of this substance become a matter of great interest in that they seem to be exquisitely favorable for nerve growth. Save for the few instances with postoperative intraneural bleeding, no large blood clot was present between the stumps, and therefore the matrix of the gap does not consist of blood plasma. The tight fit of the arterial sleeve and its sealing to the nerve by rapid clotting prevent the seeping in of extraneous fluid. This seems to leave the interior of the nerve as the sole source of whatever medium fills the gap. It may be assumed to be primarily composed of an exudate of intraneural "lymph," possibly carrying additional products exuded from the severed nerve fibers and sheath cells. The connective tissue cells in the nerve do not seem to be numerous enough to be credited with a sizable contribution. That this nerve exudate is a reality has recently been demonstrated in tissue culture experiments in which embryonic ganglions and nerves were reared at the phase boundary between a cover slip and a liquid medium. It was noted that if the medium consisted of Tyrode's solution with or without a trace of blood serum added a film of substance would seep out from the living tissue along the phase boundary and that outgrowing nerve fibers would tend to hold themselves within that film. On fixation and impregnation with silver salts, the film reveals a fine reticulated structure, which would suggest that it contains fiber proteins or other fiber-forming elements capable of oriented aggregation. While much of this work is still in the exploratory stage, it definitely points in the same direction as the splicing experiments, namely, that nerve tissue when injured produces an exudate capable of becoming oriented and obviously most favorable, in biophysical and biochemical regards, for rapid nerve growth.

The role of the colloidal matrix in which nerve growth takes place has been discussed in earlier papers.[18] The orientation of nerve growth has been resolved essentially into a matter of the orientation of the surrounding colloidal particles plus the tendency of the growing nerve fiber to comply with this orientation of its surroundings. The exudate which accumulates between the nerve stumps is evidently capable of assuming such orientation and thereby serving as an oriented guiding substratum for the outgrowing nerve fibers. In this respect it seems not to differ significantly from fibrin clots, which were used in the earlier experiments on

18. Weiss.[15] Harrison, R. G.: The Croonian Lecture on the Origin and Development of the Nervous System Studied by the Methods of Experimental Embryology, Proc. Roy. Soc., London, s.B **118**:155-196, 1935.

nerve fiber orientation and more recently by Young with good success for the union of severed nerve stumps. However, the tendency of the fibrin clot to become converted into dense connective tissue, with all the disadvantages such fibrosis entails for nerve growth, is absent in the exudate of nervous origin. Comparative studies are under way to determine whether the difference between a fibrin filling and a neural exudate in the lumen of the arterial splice is sufficiently pronounced to have practical significance.

I have said the matrix inside the sleeve is capable of becoming oriented, that is, it is presumably composed of rod-shaped polar ultramicrons. To orient these, an orienting factor is required. This factor is provided by the longitudinal tension to which the nerve is subjected. The effect of such tension on a potentially fiber-forming matrix has been described earlier.[19] It forces the ultramicroscopic fibrillar units into parallel alinement. This has two consequences: First, it compels cells of the spindle type, i. e., fibrocytes as well as sheath cells, to extend in a similar direction, and, secondly, it orients the growth of the nerve tips accordingly. In regeneration this has the effect of presenting the nerve fibers with a system of guide rails along which the outgrowing sprouts can continue in a direct straight course, passing on without obstruction into the open tubes of the peripheral stump. At the same time this longitudinal organization prevents the formation of oblique or transverse patterns which would deflect the nerve fibers from their straight course and, in addition, cause profuse branching.

Nageotte[5] has asserted that growth of sheath cells from the peripheral stump centrad precedes the outgrowth of the nerve fibers. I have made no study of the early stages of regeneration in my experiments to test this point. If it should prove correct, the orientation of the gap region would have its primary effect on the hyperplastic sheath cells in that it would force them into straight line connections between the proximal and distal stumps, which then, in turn, would serve as invasion routes for the outgrowing nerve sprouts. It is likely that the orientation of the matrix straightens nerve growth both indirectly, by way of the sheath cells, and directly, by orienting nerve fibers advancing freely. At any rate, the unconfused and strictly oriented pattern of the regenerating fibers must be ascribed in last analysis to the tension in longitudinal direction which the nerve exerts on the matrix that seals its two ends.

It may be pointed out that most suture methods in which the two stumps are united by rigid threads fail to accord the area of regeneration the benefit of this longitudinal strain. Longitudinal stresses arising in nerves held together by silk sutures are taken up by the rigidity of the suture material or at best by the rather unelastic epineurium. This leaves the interior between the ends of the suture slack, and the region which needs longitudinal strain most for a good orientation of nerve growth has the least of it. The plasma suture of Young and his co-workers is the only other method in which the gap region is accorded the full advantage of longitudinal stress in the nerve. However, since such tension, while highly desirable for regeneration, is undesirable during the early stages of suture in that it may rupture the fresh union, the fibrin method has its well recognized limitations. The arterial splice, on the other hand, in providing a firm seal between the arterial segment and the two nerve stumps, yet being elastic enough to withstand considerable extension, reduces the danger of rupture while allowing full play to the orienting action of longitudinal strain.

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19. Weiss, P.: Functional Adaptation and the Role of Ground Substances in Development, Am. Naturalist **67**:*322-340, 1933*; footnote 15 *b*.

It must be kept in mind that the favorable results thus far obtained with this method have been proved valid only within the limits within which they have been tested, namely, for the nerves of the rat, which are comparatively small. How the method will work out with larger nerves and in higher mammals, including man, is a question that cannot be answered until the results of an extensive series of experiments being carried out at the present time have become known. But it is obvious that even if the method should fail on large nerves, it is still uniquely suited for the mending of small nerves which defy ordinary suture methods on account of their small caliber.

For reasons already mentioned the method is not indicated for reunion of severed nerves in cases in which either loss of substance or considerable retraction of the stumps has created a sizable gap. To repeat, the arterial sleeve does not serve as a conduit for nerve fibers over appreciable distances, although it does help to bridge small gaps, of a few millimeters, or, in terms of the size of the nerve, a length not exceeding the diameter. In the case of larger gaps, nerve grafts will have to be used as heretofore. Again, however, the union between the graft and the two nerve stumps is to be effected with the aid of arterial splices, one such splice uniting the proximal end of the graft to the proximal stump and the other the peripheral stump to the distal end of the graft. The longitudinal stress on the nerve tends to prevent the formation of a glial scar, fibrous ingrowth and constriction at the distal suture line, so that by the time the regenerating nerve fibers have reached this level they should find a smooth and well organized pathway for transit into the peripheral stump, instead of the impassable fibrous bulkhead often encountered at the distal suture line. Experiments to demonstrate this point are under way.

A point of great practical significance is the choice of the artery. The importance of correct caliber has been previously discussed. Another feature to be considered is the amount of musculature in the arterial wall. What is really needed for a successful splice is merely the tough and impenetrable layers of elastic tissue. It is to these that the artery owes the properties that make it so suitable for the purpose. The muscular tissue, if anything, is harmful. While no detailed study has yet been made of this point, it seems that the circular musculature of the artery may receive reinnervation from autonomic fibers in the region of the wound and resume contractions. Even without such innervation a spasm of the muscular wall could develop which would strangle the nerve in the arterial lumen. As a matter of fact, the constrictions described as causes of failure were probably in part due to a secondary reduction of the arterial lumen by the contraction of the muscular coat. Pending a more systematic investigation of the subject, it may be said, therefore, that an artery will be the better suited for the purpose of splicing nerves the smaller the amount of muscular tissue in proportion to the volume of elastic tissue present.

Veins do not seem to be the equal of arteries as splicing agents. Their wall easily becomes porous and pervious, with all the detrimental consequences to nerve regeneration discussed for accidentally perforated arteries.

Experiments exploring the possibility of using arteries stored in various ways are under way. The use of arteries fixed by ordinary histologic means, as with alcohol or solution of formaldehyde, is contraindicated. Such preserved arteries have been used repeatedly in the past for the purpose of "tubulating" nerve regeneration, but the loss of elasticity caused by the treatment makes such tubular fragments wholly unsuitable for the purpose of splicing. Means by which arteries can be stored under sterile conditions for long times without losing either their elastic properties or their laminated texture, both of which are prerequisites for successful splicing, will be reported on a later occasion.

SUMMARY

A method is reported by which severed nerve stumps can be united without the use of sutures. It consists in sealing the nerve ends into a common tightly fitting sleeve of live artery. Histologic evidence is presented, based on experiments on rats, showing that when this method is used (1) a firm tie between the stumps is obtained which has adequate tensile strength and offers most favorable conditions to nerve fiber regeneration; (2) nerve fibers regenerate in straight parallel courses; (3) regenerating fibers do not branch, nor do they stray about, intermingle, escape from the nerve or form local neuromas; (4) regenerating fibers essentially retain their mutual topographic relations; (5) ingrowth into the nerve of fibrous connective tissue and strangling of nerve fibers by fibrosis are prevented; (6) no fibrous scars form at the suture lines, and (7) even the smallest nerves can be mended.

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