

## Original Articles.

### RECENT EXPERIMENTAL WORK ON THE "FUSION" OF NERVES AND ITS PRACTICAL BEARING ON INFANTILE PARALYSIS. REPORT OF A CASE OF INFANTILE PARALYSIS TREATED BY THIS METHOD.\*

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THIS evening I wish to address you on a subject which I must confess is still imperfectly clear in my own mind, but, on account of the suggestiveness of certain facts that have been brought out in my research, I feel that it might perhaps interest you if I presented a brief summary of certain aspects of the work, so far as it has progressed.

Therefore I wish this report to be regarded as preliminary only, hoping that at some later time I shall have the opportunity to present to this same section the salient points with greater clearness and conviction.

Before it is possible for me to explain the term "nerve fusion," it is necessary briefly to define certain other terms that I am obliged to use. First the term, "nerve pattern." The nerve pattern is simply the anatomical arrangement or grouping of the fibers in the cross-section of a nerve. This arrangement of the fibers has a definite relation to their peripheral distribution. Thus the main trunk of the sciatic, studied high up, consists for the most part of two large funiculi, one of which is destined to become the external popliteal nerve and the other, the internal popliteal nerve. As we follow the nerve down, each of these two trunks is found to redivide into smaller branches, each branch representing the ultimate distribution of the fibers to certain muscles, skin areas, etc.

(Although it is possible by such a cross-section of a nerve to understand the significance of its component parts as regards distribution, it is not possible to recognize from this aspect alone what the function of the individual fibers is, namely, which are motor, which sensory, which vasomotor, etc. To be sure, there is a rough distinction based upon the size of the fibers, the motor fibers usually being quite large and the vasomotor fibers quite small, but as they are all mingled indiscriminately in the individual funiculus, the nerve pattern gives us but little information as to this point.)

Although the main nerve trunk divides into branches and the branches redivide into others, it is not to be supposed that the individual fibers themselves form any division; each fiber is a single branch of a neurone and remains so all through its course. It begins as an axone from its cell of origin in the gray matter of the cord or a ganglion, and, although in its route it may be subject to the many relational diversities as it passes through spinal root, plexus, nerve trunk and peripheral branch, it forms no break or

division in itself until it finally arrives at its place of peripheral distribution in its respective end organ, muscle, skin-area or blood vessel. Thus we see that the nerve pattern may change continually as we follow the nerve down toward the periphery, although each fiber maintains both its anatomical and physiological integrity in relation to a given cell.

In considering the subject of anastomosis of nerves, Stoffel<sup>1</sup> recently demonstrated the necessity of distinctly and definitely understanding the nerve pattern of normal nerves. By a series of gross dissections in hardened nerves of a human infant, he worked out the nerve patterns or the topography of the cross-section, as he referred to it, of some of the larger nerves, such as the median and sciatic. That his point is well taken, there can be no question. I mention it here because it suggests one of the main problems with which we are obliged to deal, and this problem is whether we can artificially change the nerve pattern. Such authorities as Langley and Anderson, Kilvington and Osborne and others have maintained that the pattern can be changed under certain conditions, and they refer to such a change of pattern as a nerve distortion. The object of a nerve distortion is apparent. It is hoped by such a means to redistribute fibers which supply a set of muscles or other tissues in such a way as to increase their functional value.

It goes without saying that a change of nerve pattern or a nerve distortion cannot be obtained without, temporarily at least, seriously disturbing the nerve tissues at the point where the distortion is desired, and we must consider the methods by which such a distortion may be gained. I know of only two such methods; one I have already referred to, namely, nerve anastomosis, which consists in suturing different nerves together so as to form new combinations, and the second is the method of which I wish to speak more especially this evening, namely, that of nerve "fusion."

Before defining the term nerve "fusion," it is necessary for me to say a few words as to the salient features of nerve regeneration after division or crushing, because the important points in nerve fusion depend upon certain anatomical features in this process. It is well known that division of a peripheral nerve is followed by a very characteristic process below the point of division. Clinically, the striated muscles supplied by the nerve no longer respond to the will. Experimentally, after the first few days the peripheral stump loses its reaction to mechanical and electric stimuli, and anatomically, after the first week or so, one finds in the stump below the division that the myelin sheaths have broken up, that the axis-cylinders no longer stain and that there takes place within the scar a marked proliferation of cells and nuclei. These proliferating cells are supposed to be from the sheaths of Schwann. Still later the myelin completely disappears and the main characteristic of the scar in the nerve is simply the increased number of cells just

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<sup>1</sup> Zeitschr. für Orthop. Chir., Bd. 25, 1910.

referred to. If the separation between the two divided stumps is maintained, some regeneration in the fibers of the peripheral stump will take place, but only up to a certain point, which varies under local conditions. We may ascribe such beginning regeneration to the part taken by collateral nerves which were divided during the original operation and which now offer the fibers in the peripheral stump a new central connection. But practically speaking, we may regard a nerve cut off from the central stump as sufficiently degenerated to deserve the name. Supposing now that instead of trying to keep the stumps separated after division, we resuture at once or, what amounts to the same thing, we tie a ligature about the nerve and immediately remove it. At first the result is just the same as described above in the peripheral stump, but presently we note a great change, for regeneration of the fibers occurs to a marked degree and if the scar is not too great, the process will in most cases go so far as finally to develop a perfect nerve, physiologically and anatomically.

As to the scar that forms at the place of division under this condition of immediate approximation of the stumps, very clear descriptions of its essential features have been offered by those who have studied this subject most deeply, including such authorities as Ranvier, Cajal, Perroncito, Neumann, Stroebe, Bethe and others. Although these authors disagree materially in their interpretation of certain features, they do agree in most of the essential anatomical facts. The first important fact is the proliferation of the nuclei of the cells of Schwann, which I have mentioned above; axis-cylinders, myelin sheaths and other component parts of normal nerve fibers, including the perineurium of the funiculus, practically disappearing in this mass of new cells. These cells are elongated and run in every direction. On account of this proliferation of tissue the nerve here forms a swelling which is sometimes referred to as a bulb or a neuroma. The length of the bulb indicates the length of the scar. Weeks later, the bulb contracts and approximates the size of the normal nerve, and in its interior, regeneration begins from the central stump, the axis-cylinders pushing their way among the proliferated cells and becoming surrounded with new myelin which, in all probability, is also of central origin. Regeneration meanwhile may make some headway in the peripheral stump, and by some process which is not yet definitely understood the regenerated fibers from the central stump passing through the scar join those in the peripheral stump, or mingle with them so as ultimately to form a new and continuous nerve with every anatomical and physiological feature of normal nerves.

I wish now to call your attention to four distinctive points in the formation of this scar which are pertinent to the present problem. In the first place, the perineurium and endoneurium of the crushed nerve are lost in the proliferated mass of cells. Secondly, when the fibers begin to redevelop they do not develop in straight lines

or in parallel lines so as to follow the direction that they had in the central stump, but for a considerable time at least they mechanically follow the course laid down by the arrangement of the cells in the scar, and this means that they run in every direction—downward, upward and obliquely and cross each other frequently (Perroncito, Stroebe, Neumann, etc.). This is an extremely important point. Thirdly, as the regenerating fibers push their way between the cells, they present peculiar endings, often forming fibrillæ which branch from various parts of their growing ends (Ramon y Cajal, Poscharissky, Perroncito). Fourthly, and later in the process, these same fibers are seen to rearrange themselves in an extraordinary and striking manner. From the indiscriminate positions which they were obliged to take on account of the mechanical conditions of the proliferated cells, they now form into straight and parallel lines, conforming to their respective beginnings in the central stump. In a word, in the last stage of regeneration in the scar, the nerve fibers tend to form into their original nerve pattern. But not only do the nerves tend to take their original nerve patterns in the scar, but as they pass through it they also tend to seek out their original tracts in the peripheral stump, and this means that each fiber, whether motor, sensory, vasomotor, pilomotor or secretory, takes up its original function. This tendency is usually ascribed to chemotaxis (Langley). Thus we see that the direction of the new fibers in the scar is influenced by two factors according to the stage in the process; first, the factor of new cell formation which guides the fibers in every direction, and later, the factor of chemotaxis which tends to send the fibers into parallel directions and into their original tracts.

Having shown in this summary fashion the salient features of the scar in a divided nerve, I believe you will now be able to understand what I mean by nerve "fusion." Nerve "fusion" is nothing more nor less than a method which attempts to render permanent the arrangement of the fibers in that stage of regeneration when they run in more than one direction. It is a method for taking advantage of the confused nerve pattern of the scar in the transitory stage and fixing that pattern in the hope that, when regeneration is finally completed, the fibers will have grown down different tracts from those which they originally occupied, thus defeating chemotaxis. So in a case of paralysis, if some of the fibers in the nerve are degenerated and their sheaths are empty, the question arises whether the interposition of a proper scar in the course of that nerve may distort its nerve pattern so as to enable the empty tracts to become occupied again with new fibers. Not only this, but we may also inquire whether some of the branches that form on the sprouting ends of the divided axis-cylinders may also be made to enter tracts which have previously been empty, thus gaining not only a new distribution of fibers, but also an actually greater number.

The theoretical basis of nerve "fusion" being

made plain, the next question is, What method may we use to obtain and maintain a pattern of such peculiar characteristics? Before speaking of this method, I must mention one other point which is based upon the researches of others. This point is that the length of the scar is of great significance in governing the amount of regeneration (Howell and Huber, Perroncito, etc.). Thus it is known that a very short scar such as may be obtained by good approximation of the nerve ends will not change the nerve pattern, and that too long a scar will practically prevent regeneration, because of the interposition of too much mechanical resistance. This point, — the length of the scar, — therefore, was a suggestion to begin with, and the thought was not far removed to use ligatures to obtain fusion. With ligatures we could not only crush the nerve so as to produce the necessary scar, but by using more than one we could control the length of the scar by the distance that they were placed apart. Such ligatures, moreover, enabled us to gather more than one nerve into the formation of the new pattern. Finally, by using ligatures of absorbable material, namely, catgut, we could keep the crushing factor under surgical control from the point of view of time, because such a ligature disappears after a few days. In this way the method was evolved and this method consists simply in tying one or more nerves with two catgut ligatures with the intention of producing a sufficiently long scar to cause distortion of pattern. In order to be sure that crushing was produced, we applied a hemostat to the nerve between the ligatures. The ligatures have been placed  $\frac{1}{8}$  to  $\frac{1}{4}$  inch apart.

As regards the plan of our experiments we have tried several, the two chief ones being, first, the fusion of two adjoining nerves where one has had a large piece excised above the fusion, and, second, the fusion of two adjoining nerves without excision. We have usually worked upon the popliteals because they are easy to approach and supply antagonistic muscles. The animals used were chiefly full-grown dogs. We let the animals run three or four months before testing them.

These tests have been made from two points of view; first, from the point of view of regeneration, and, second, from the point of view of the crossing fibers. As regards the tests for regeneration, it may be stated that our evidence has most clearly shown that it does take place to a marked degree, but of course not in every case. These tests have been clinical, physiological and anatomical.

As regards the tests for nerve crossing, we have been guided, in a measure, by the work of Kilvington and Osborne, who have done their experiments by the older method of combining nerves by suture. Although in a number of cases we have found that impulses will apparently pass through the scar from one nerve to another, we have not been able, as yet, to rule out electrotonus, for we feel that the currents used have been rather too strong. Even so, our negative results are far more numerous than our positive ones.

From the anatomic point of view, however, we have demonstrated that the fibers actually cross. But we have not been able to obtain all positive tests in a given case, one case showing histological crossing and no return of function, another showing return of function but no experimental evidence of crossing, etc. Nor have we been able to show, at least to our own satisfaction, that the redirection of the fibers which we can demonstrate anatomically at certain stages remains permanent. Some of the preparations are, however, extremely suggestive, and, taken as a whole, I believe that we have sufficient evidence to justify us in making further experiments along this line.

Besides doing these experiments on normal nerves, we have also been engaged in disturbing the nerve pattern after lesions had been produced in the spinal cord by earlier operations, hoping that by thus emptying some of the nerve tracts by a central lesion we might in the second operation so distort a nerve trunk as to fill up these empty tracts. We have also experimented on the anterior roots directly, and in other cases on the cauda equina, with special reference to paralysis of the tail. The account of these experiments must be postponed for special reports; I merely mention them in passing in order to indicate that the question of nerve "fusion" is not yet solved, even if one can prove that the nerve pattern in the normal can be altered, because after an original paralysis you must deal not only with degeneration of fibers, but also with fatty degeneration of the muscles originally supplied by those fibers, to say nothing of the fact that the empty tracts after a long-standing paralysis tend to become occluded by connective tissue and later to disappear entirely.

Of course the great practical import of such work as nerve "fusion" and nerve anastomosis is its bearing on infantile paralysis. Much has lately been written upon the pathology of this disease, but the points which are of essential importance from a surgical point of view have been known for some time. These points are that the disease affects chiefly the anterior horns of the gray matter, causing a degeneration or disappearance of the ganglion cells located there, with a resulting paralysis which is chiefly motor.

As regards nerve "fusion" for this condition, we can at once see that theoretically the operation might prove to be of value. It is, of course, a grave question as to whether there is any hope if the muscle tissue is degenerated beyond a certain degree, so that the time interval after the original paralysis might prove to be of great importance in considering the fusion; moreover, it cannot be expected that such a procedure could be helpful in every case. But, generally speaking, there are at least theoretical grounds for thinking that nerve "fusion," if properly done, might in selected cases be of some benefit.

As regards the comparative value of ordinary nerve anastomosis by suture with nerve "fusion" as we have described it, I would not like to make any important comparison at present, except to

say this: that although there is no question as to the theoretical value of the older method, such a method would seem to be much more limited in its applicability than the one I have just described, because that method (nerve anastomosis by suture), to be intelligently done, implies an accurate and definite knowledge of the cross-section topography of the nerves, and this knowledge is usually difficult and often impossible to obtain. Nerve "fusion" does not require this. Besides this seeming advantage of "fusion" over suture where two or more nerves are brought together, nerve "fusion" in addition aims to distort the pattern in the individual funiculus, even without the help of a second nerve. This may prove to be of importance. I might also add that on account of the immediate degeneration below the scar it does away with temporary activity of such muscles as may be producing deformity on account of contractures, thus serving the purpose that a tenotomy might serve in other cases; thus while the nerves below the scar are temporarily out of commission, the limb may be placed in a neutral position of best function so that when regeneration is complete, such deformity as existed becomes obliterated.

The work which I mentioned has been in progress for several years, and from our experiments it seemed that we had sufficient grounds to justify us in trying a nerve "fusion" in at least one human case. Such an opportunity arose last fall. The case I chose was not on account of its favorable characteristics, but one which was in a measure quite unfavorable, — the paralysis was not recent and only one important muscle had preserved anything like its normal integrity.

#### REPORT OF THE CASE.

This case (Y. C.) first seen Aug. 25, 1910. Nothing important in the family history. Child was learning to walk at the age of nine months, when she was taken with an illness lasting about six weeks, losing the use of her legs. Eighteen months later started to walk again and has remained in a crippled state up to the present time, limping badly. Is wearing store braces.

Sept. 16. — Examination.

*Status.* — Well developed and nourished except for legs, which show evidence of paralysis. Patient is very lame but can walk alone. (The left leg shows control of the hip. She can hold the knee extended, but only in external rotation. Hamstrings under control. The foot in a position of equinus of 45°, the tendo achillis being drawn. She can flex and extend the toes and can evert the foot. No power in inversion or dorsal flexion.)

*The right leg.* — She can control the hip and extend and flex the knee in practically normal fashion. She can dorsal flex the ankle and can extend and flex the toes. She seems to have no other control of this right ankle. The foot can be put into marked calcaneus although no permanent deformity has yet resulted. The foot can be extended to only a right angle at the ankle. Stimulation of skin with sharp point over same lower leg and foot shows no anesthesia. This same (right) lower leg examined further with faradic current, using a du Bois Reymond coil (Ludwig) of the vertical type with 10,000 windings of the secondary and a one-pint Daniell cell, and shows the following: The only motor point found is that of the tibialis

anticus, half way down the front of the leg. Minimum stimulation for this muscle obtained with secondary at 123 mm. No motor point could be found for the long extensor of the toes, but occasionally with strong stimulation over belly of muscle the toes would dorsal flex. Currents over soleus-gastrocnemius and tibialis posticus so strong as to be unbearable on the observer's fingers produce no response in plantar flexion or inversion respectively. Touching electrode to the sole causes flexion of toes. No response was obtained in the peroneal muscles. Stimulation over peroneal nerve occasionally causes dorsal flexion of ankle.

Knee jerk sluggish on the left and lively on the right.

*Measurements.* — Anterior superior spine to internal malleolus, right, 19.5 inches; left, 19 inches. Circumference of thigh at perineum, right, 11 inches; and left, 10 inches. Circumference of calf at maximum point, right, 6½ inches; left, 7 inches.

The most suggestive thing which can be obtained in the right lower leg is the loss of power in the gastrocnemius-soleus and tibialis posticus, suggesting a marked paralysis of the internal popliteal.

Sept. 17. — Ether operation at Lakeside Hospital (service of Dr. D. P. Allen): Incision 2½ inches long made on the back of thigh of the right leg, the lower end of the incision being 2 inches above the knee-joint. Biceps freed and the sciatic exposed. At the place exposed, sciatic could be separated into the external and internal popliteal divisions. These two divisions carefully stroked for several minutes with a tenotomy knife until they bled profusely, then squeezed together into a pulp with a hemostat for a distance of ½ inch and tied with two sutures of plain catgut ¼ inch apart (No. 1 size). In squeezing, the ankle dorsal flexed sharply. Skin sewed with catgut. In accordance with a suggestion by Dr. Briggs, the foot was put up in equinus on account of the calcaneus tendency and the plaster run from the toes to the groin.

(On the left foot, tenotomy of the tendo achillis. The peroneus longus exposed, and by making a hole in the interosseous membrane was passed between the fibula and tibia. The tendon passed through from behind and sutured into the tibialis anticus while the latter was on the stretch, so as to hold the foot at a right angle. Tibialis anticus then shortened. Chromicized catgut used for suturing the tendons and plain catgut for the skin. Foot put up slightly within a right angle and slightly inverted.)

Sept. 18, condition good. No temperature. Toes remain pink on both sides.

Sept. 21, condition good. No temperature. On being asked to move the toes of the right foot, she fails to do so.

Oct. 29 (patient at Rainbow Cottage — Convalescent Hospital), plaster removed on both legs. On the right, wound healed by first intention. Sensation and motion tested. Sensation seems present except in the heel, where there is some callus where she does not seem to feel the point of a pin. From a functional point of view, there is no return of power. She cannot move the ankle in any direction nor can she move the toes, but the foot now readily goes into equinus, there being no longer any resistance in the tibialis anticus.

Measured for a brace with double uprights and with rigid ankle-joint to hold the foot in slight equinus. New plaster applied holding the foot in some equinus and varus.

The other foot shows healing by first intention, the foot remaining in varus. Measured for a valgus brace. New plaster. Told not to be allowed to get on her feet.

Nov. 23, child had developed some little sloughs

<sup>2</sup> For the privilege of operating on this case, the author is indebted to Dr. C. E. Briggs, acting surgeon.

on the fourth and fifth toes of the right foot. In trimming back the plaster another slough was produced. The toe sloughs have healed up and the last one is almost healed. There is no return of movement yet in the toes or in the ankle, but a peculiar resistance suggesting beginning tonicidity seems to be developing on the surface of the dorsum. At this place, when she is told to attempt movement, a faint twitching is sometimes noticed.

Dec. 2, sloughs have healed. No movement has returned. Tickling and pin pricks are certainly perceptible. Braces tried on.

Jan. 5, 1911, child wearing braces which seem to fit properly. She has no power in motion yet in the right foot. The four outer toes show some swelling and some blueness. Patient stood upon her feet and stands alone. To try a few steps.

Jan. 11, child steps very well on her feet with the braces on. No motion has come into the foot. There is now a peculiar reflex, namely, flexing the ankle causes flexion of the knee and hip. Sensation has returned well, the child feeling sharp objects distinctly.

Jan. 18, distinct motion noted in dorsal flexion. With tickling of the foot she bends her ankle up and outward a few degrees and usually flexes the four outer toes a little. After the foot comes up it goes back into a right angle, but it cannot be stated whether that is due to the elasticity of the tissues or to contraction of the soleus. Child walking a little. Measurements of calves, right,  $6\frac{1}{2}$  inches; left,  $6\frac{1}{2}$  inches.

Jan. 25, foot to-day shows a distinct improvement. She has very slight motion in plantar flexion. She has slight motion in inversion. She everts quite well and she can both flex and extend the toes. There is also noticeable a peculiar blueness of the anterior part of the foot, extending from the ends of the toes to about 2 inches back to a line where the blueness stops rather suddenly.

Feb. 7, some improvement. She now bends her ankle downwards. This movement is over an arc of  $10^\circ$ . She moves it upwards about  $10^\circ$ , inwards a few degrees and outward about  $20^\circ$ . Her toes can be moved upward and downward. Compared with her condition before the operation she has all the motions of the ankle and foot, and the total amount represented is about the strength represented in the tibialis anticus before the operation. At the present time the tibialis anticus does not stand out, out of proportion to the other muscles. The color in the front part of the foot is much like normal, the blueness having disappeared.

Feb. 16, case brought into the experimental laboratory and the electrical tests tried. The skin, however, was very sensitive so that the tests had to be postponed. Motion tested again. She can evert, plantar flex, and dorsal flex about  $15^\circ$ . Inversion is less. Circumference of calf,  $6\frac{1}{4}$  inches.

In presenting this case only the facts are submitted and no definite conclusions are as yet to be drawn. One thing may, however, be stated with reasonable assurance, namely, that the control of the patient's ankle is now different from what it was before the nerve fusion, although the total amount of power is as yet no greater. A final verdict can only be given when she reaches that stage where no further improvement is going on, when a supplementary report of the case will be made.

In closing, I wish to acknowledge the important assistance which has been rendered to me by Prof. Geo. N. Stewart, director of the laboratory,

and Dr. Marine, also of the laboratory. The former has made many valuable suggestions in the physiology of the research, and the latter has done the same from the anatomical point of view.

## A CASE OF HEMIATROPHY FROM SCLERODERMA.\*

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WHILE a moderate amount of asymmetry between the two halves of the body is an ordinary condition, the more extreme degrees, an actual hemiatrophy, are comparatively rare. Congenital hemiatrophy, as a rule, is due to some malformation or defective development of one half the brain occurring in fetal life. Acquired hemiatrophy, which is far more common, is generally due to some cerebral lesion occurring in childhood and is ordinarily associated with infantile hemiplegia. It may also happen that anterior poliomyelitis affects the arm and leg on one side, giving rise to a partial hemiatrophy, but this is rare.

Probably the rarest form of hemiatrophy is that associated with scleroderma, of which I have been able to find only six reported cases. It seems justifiable, therefore, to present this additional case, which is, so far as I know, the only one reported in this country.

David B., aged eighteen, single, a native of Boston, presented himself at the neurological service of the City Hospital in April, 1907. Except for a little "rheumatism" on the father's side, the family history was not remarkable. He had always been well, except for measles and scarlet fever in childhood. He had never used alcohol or tobacco and denied any venereal disease.

He had worked for two years as a metal-worker, handling tin and sheet-iron, but not lead. Two years before coming to the hospital he had had some sharp paroxysmal pain in the left leg, followed by spasmodic clonic contractions of the muscles of the thigh and slowly progressive wasting of the whole leg. At about the same time he noticed some pigmented nodules in the skin on the left side of the epigastrium, on the anterior aspect of the upper third of the left thigh, just below the knee and along the lower inner border of the gastrocnemius. For six months he had had some "drawing" sensations and spasm near the sternal attachment of the abdominal muscles, and for two weeks some spasm and weakness in the left upper arm, especially in the biceps. The left leg had grown progressively weaker. Except for the symptoms above noted, however, he was in good health and able to work regularly. Occasionally, if he kept one position too long or worked in a cramped position, the leg would give out for a few minutes. There was no headache, vertigo or visual disturbance. He slept

\* Case presented at the joint meeting of the New York and Philadelphia Neurological Societies with the Boston Society of Psychiatry and Neurology at Boston, Nov. 23, 1907, and at a clinical meeting of the Neurological Section of the Royal Society of Medicine in London, Dec. 15, 1910.