GUIDES FOR NERVE REGENERATION ACROSS GAPS*

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The problem of how to bridge nerve gaps that cannot be further reduced by manipulative procedures (mobilization, rerouting, stretching, etc.) has not yet been adequately solved. The results of nerve grafts in man have been disappointing and though improvements in technique or the use of devitalized undenatured grafts might yet bring better success, the prospects are so uncertain that it is indicated to explore other alternatives. Several attempts in that direction have been made in the past. Various tissues, living or fixed, as well as artificial structures, organic or inorganic, have been tried as guides for regenerating nerve fibers, mostly without significant success. As has been pointed out in a recent review of this subject by Weiss,12 most of the former failures can be explained by errors of technique, often based on misconceptions about the mechanism of nerve regeneration. We have, therefore, continued the search for improved methods on an experimental scale, and the results are summarized in this article.

On a previous occasion,12 brief mention was made of experiments on the bridging of nerve gaps by arterial tubes filled with blood. While resembling superficially some older methods of "tubulation," these experiments observed more closely the known requisites of nerve regeneration, and hence, yielded markedly better success. A more detailed account of these experiments is presented in the following.

TUBULATED BLOOD BRIDGES IN THE RAT

Pieces were cut out from various nerves of rats (sciatic, peroneal, vagus) leaving gaps of about 10 mm. in length. The nerve ends were then fitted into a tube of artery of proper length and width by the technique described previously. The empty part of the tube was then filled with blood or some other medium to be tested, guarding against the introduction of air bubbles. Experience has shown that fillings of Ringer's solution or blood plasma lead to fibrosis with obstruction of nerve regeneration. Therefore, only gaps filled with whole blood will be considered here.

Seven rats thus operated upon were biopsied after from 4 to 17 weeks. The experimental nerves were studied histologically (Bodian's silver impregnation). In the older cases, recovery of function had occurred but was decidedly inferior to that observed after end-to-end union or even after the use of frozen-dried grafts. Aside from technical accidents (slipping of one of the nerve ends from the tube in one case), the method had inherent defects, which were revealed by the microscopic study.

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In a number of cases, the blood-filled part of the artery had collapsed, presumably because of leakage; the wall was creased longitudinally, with practically no lumen left. A narrow strand of dense connective tissue, sometimes containing a large longitudinal blood vessel, occupied the limited central space, and regenerating nerve fibers had not been able to penetrate it.

In cases in which the lumen had remained wide open, nerve regeneration across the gap had proceeded satisfactorily for varying distances, but then been impeded by islands of heavily fibrosed or areolar tissue. As already noted in previous similar experiments,17 the orientation of the cellular strands and nerve fiber bundles was remarkably straight.

On the basis of earlier experiments,16 we thought that the formation of fibrous blocks could perhaps be prevented by increasing the fibrinolytic potency of the initial clot through the admixture of large masses of leukocytes, taken from theuffy coat (stratum between red cells and plasma) of centrifuged homologous blood.

**TUBULATED BLOOD BRIDGES IN THE CAT**

In five cats (F7-11), pieces were cut out from the tibial or peroneal nerves in midthigh, leaving the stumps after retraction separated by gaps of 20, 18, 10, 28 and 25 mm., i.e., fifteen to thirty times as long as the width of the nerves. The ends were introduced into a matching segment of carotid artery, which was then filled with the modified blood. Except for cat F11, in which one nerve end was found at autopsy to have slipped out, the operations and subsequent recovery histories were satisfactory. Brief case descriptions follow.

_Cat F7_. Gap in tibial nerve, 20 mm. long, bridged with carotid artery (kept refrigerated in Ringer’s solution for 3 days), filled with blood plasma and erythrocytes from centrifuged heparinized blood in a volume ratio of 2:1 and an added amount of buffy coat.

At 58 days p.op., the gastrocnemius was well palpable, but active function was doubtful. Active plantar flexion was definitely present at 105 days p.op.; it was still subnormal in strength at 202 days, but well recovered after one year; even then, the animal, digitigrade for most of the time, would occasionally relapse into a few plantigrade steps.

At biopsy (308 days p.op.), the artery was found to have narrowed so as to cause a “bottleneck” with consequent bulbous enlargement of the proximal stump; there was no distal swelling. The muscle weights were 27.8 gm. for the tibial group, and 8.3 gm. for the peroneal group. Since the opposite leg had been subjected to another operation, it could not be used as control for muscle weights. But the weight ratio of 3.35 between tibial (reinnervated) and peroneal (undisturbed) muscles in the experimental leg is approximately the same as that of normal legs, hence indicates full weight recovery of the reinnervated muscles.

Microscopic examination: The nerve in the area of the former gap has a characteristic pattern, differing from that observed after regeneration over short gaps,9 but even more strikingly from that noted in gaps filled with scar tissue. It differs from the former in that it is less well oriented and contains more connective tissue, but its constitution is much nearer that of normal nerve than would ever be obtained in ordinary scar tissue. The regenerated nerve fibers are grouped into large bundles which are separated by partitions of connective tissue thicker than regular perineurium. The general direction of these bundles is longitudinal, but not straight; they interweave and give the nerve a braided appearance. Fig. 1 shows a longitudinal section through this region. The most significant difference between this type of regeneration and that in ordinary scars is that the nerve fibers are assembled into well