Functional Nerve Regeneration Through Frozen-Dried Nerve Grafts in Cats and Monkeys.

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Functional Nerve Regeneration Through Frozen-Dried Nerve Grafts in Cats and Monkeys.*

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As reported previously,[1] grafts of frozen-dried and rehydrated nerve in the rat form excellent conductors for regenerating fibers. Extension of these experiments to cats and monkeys has given the following results. Six of 10 cat grafts and 21 of 36 spider monkey grafts have thus far been examined functionally.

Material and Methods. The nerves, either intact or predegenerated, were frozen in Isopentane at approximately −150°C, dehydrated over P_2O_5 *in vacuo* for one week, sealed, stored for from 2 to 4 months, and then rehydrated in Ringer's solution *in vacuo*. Segments of from 1 to 3 cm in length were used to bridge corresponding gaps in the tibial or peroneal nerve severed in the middle thigh. The grafts were joined to the stumps by sleeves of fresh or frozen-dried artery. Heteroplastic frozen-dried grafts (from macaque or cat to spider monkey) were used in some instances. Some grafts were not connected with the stumps immediately but first allowed several days of local conditioning at the site of the lesion. Occasionally multiple grafts were used, either in parallel or in tandem. Grafts must not be stripped of their perineuria.

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[1] Weiss, P., and Taylor, A. C., PROC. SOC. EXP. BIOL. AND MED., 1943, **52**, 326.

FIG. 1.
Cat tibial nerve 6 months after receiving frozen-dried graft. Bodian impregnation. ×7. Proximo-distal direction from top to bottom. Splicing arteries are marked by brackets, the approximate extent of the graft (consisting of double nerve) is marked by a solid line. Asterisks indicate flaws due to histological sectioning. Note absence of "suture lines."

Results. A. Cat. Motor recovery of the peroneal nerve, as tested by dorsiflexor and toe-spreading reflexes, began at 3 months, and was nearly complete at 5-6 months after the operation. Fig. 1 illustrates full histological restitution of a tibial nerve through a 17-mm frozen-dried graft, 5 months p. op. (The peroneal nerve of this specimen had likewise received a graft.) Functional recovery had been clinically complete and the combined weight of the reinnervated leg muscles was only 6.5% below that of the intact control side. Fiber caliber and myelinization have well recovered at sample levels of 50 and 130 mm regeneration distance (Fig. 2).

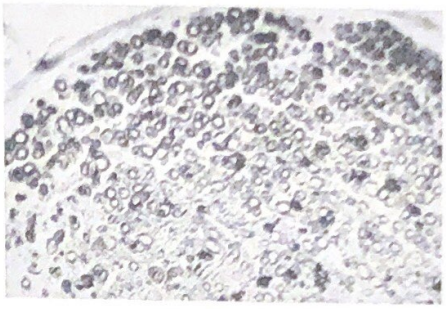

FIG. 2.
Cross section of regenerated portion of nerve of Fig. 1; 5 cm distal to graft. Osmic acid. × 120.

B. Monkey. Motor recovery was tested both by observation of spontaneous and reflex function and by electrical stimulation of the exposed nerves. Of 21 nerves examined between 5½ and 10 months after the operation, functional restoration was excellent in 8, good in 4, fair in 3, poor in 2 cases. Total failure in 4 cases has been accounted for by faults of technic. An interpretation of the variability of the results will be given in a later report in connection with the histological findings. Full recovery has occurred after the use of homoplastic grafts, as well as macaque-to-spider grafts, in the latter case with perceptible delay. Success with cat-to-monkey grafts was negligible. In a fully recovered homoplastic test case, electric shocks to the peroneal nerve proximal to the graft site gave strong contraction in intrinsic foot muscles, at 320 mm regeneration distance, when tested 182 days after the operation; this means that regeneration had proceeded at a minimum daily average of nearly 2 mm including the graft and its junctions.

No constant differences between predegenerated and non-predegenerated, or between conditioned and unconditioned, grafts have as yet been ascertained, although such differences might be expected in view of the fact that the "devitalized" grafts are being repopulated by host cells. As in nerve grafting in general, success depends on the proper way of joining the graft to the stumps. The method of sutureless sleeve-splicing[2] has been instrumental in securing the success of the frozen-dried grafts in the present experiments.

Summary. Full functional recovery may be obtained in cats and monkeys after the bridging of a nerve gap of several centimeters by grafts of frozen-dried nerve, stored for several months and rehydrated before use.

[2] Weiss, P., PROC. SOC. EXP. BIOL. AND MED., 1943, preceding paper.