

are:² to align the nerve ends; to permit longitudinal stress to act on the "scar"; to prevent dissipation of fibrinolytic agents from the gap and thus insure proper liquidity of the "scar"; and to keep fibrous tissue and other local growth from penetrating. Continued research may yet produce a synthetic sleeve answering these demands.

For end-to-end reunion of stumps under tensions greater than an arterial cuff can hold, means must be devised to reconcile the need for forcible approximation with the cardinal precept for good regeneration, viz., to keep the zone of union free from artificial intervention, particularly sutures. A solution may lie in approximating the stumps by means of a permanent loop of Tantalum or Columbium wire, stitched either through the nerve stumps or the epineuria at considerable distance

(more than one inch) from the cuts, and then splicing the free ends with an arterial sleeve just as in unstretched unions. It may be expected that the gradual "give" at the points of attachment will place enough strain on the young tissue connecting the stumps to produce in it the desired longitudinal organization. Results of this operation will be reported on a later occasion. Experiments are also under way to determine the maximum length of a blood filled gap between stumps compatible with optimal nerve regeneration.

Summary. Results obtained with sutureless nerve reunion by means of cuffs of live or frozen-dried artery in 21 rabbit, 30 cat, and 81 monkey nerve splices have confirmed for the larger mammals the conclusion previously reached in the rat, that optimal nerve regeneration may be secured by this method.

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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.

* This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago; also aided by the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago. The monkey experiments were carried out at the Yerkes Laboratories of Primate Biology, Orange Park, Florida, and I am greatly indebted to Dr. K. S. Lashley for his generous contribution of laboratory facilities. Technical assistance by Dr. R. W. Sperry and Dr. A. C. Taylor is also gratefully acknowledged.

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

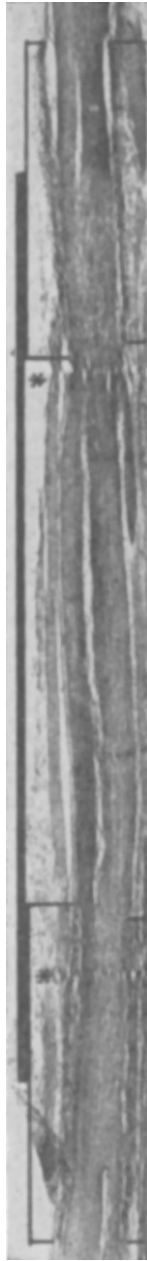


FIG. 1.

Cat tibial nerve 6 months after receiving frozen-dried graft. Bodian impregnation. $\times 7$. 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 myelination have well recovered at sample levels of 50 and 130 mm regeneration distance (Fig. 2).

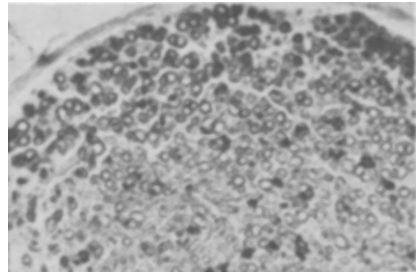


FIG. 2.

Cross section of regenerated portion of nerve of Fig. 1; 5 cm distal to graft. Osmic acid. $\times 120$.

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-splicing² has been instru-

mental 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.

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Neurotropic Virus Infections in Chicago, 1939-1941. Nine Cases of Lymphocytic Choriomeningitis.

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Ordinarily it is difficult or impossible to diagnose the various neurotropic virus infections of man on the basis of clinical or pathological findings because of their great similarity. For this reason, laboratory procedures must be employed for identification of the specific virus. During epidemics, it may be possible to identify such infections as poliomyelitis by means of characteristic findings. On the other hand, laboratory diagnosis becomes mandatory if two or more viruses are known to be endemic in the same region. Thus mixed epidemics of St. Louis encephalitis and western equine encephalomyelitis have been reported in certain of the Western states.¹⁻³ Laboratory aid is also essential for the diagnosis of lymphocytic choriomeningitis because of the protean clinical manifestations this virus produces and the fact that this infection is highly sporadic in man.⁴

The present studies were carried out in order to identify possible etiologic viruses in 75 patients suffering from various sporadic central nervous system infections in the Chicago area. In most instances, specimens of both spinal fluid and defibrinated blood obtained during the acute stage were routinely inoculated into Swiss mice and guinea pigs. Blood specimens were defibrinated by means of glass beads. In fatal cases, small portions of tissue obtained from different areas in the brain and cord were triturated in a mortar with sand, and a 10% emulsion in buffered saline (pH 7.4) was prepared. Most specimens were inoculated into animals within an hour after collection from the patient. Usually each specimen was inoculated intracerebrally (0.03 cc) into each of 6 mice and both intracerebrally (0.2 cc) and intraperitoneally (1 to 4 cc) into each of 2 guinea pigs. All animals remaining normal for 30 days after the original inoculation were tested for immunity to lymphocytic choriomeningitis by intracerebral inoculation with approximately 10 MLD of known virus. Bacteria were ruled out by routine inoculation of various aerobic and anaerobic culture mediums. Evidence that our stock mice and guinea pigs were free from latent infection with the choriomeningitis

¹ Howitt, B. F., *Am. J. Pub. Health*, 1939, **29**, 1083.

² Meiklejohn, G., and Hammon, W. McD., *J. A. M. A.*, 1942, **118**, 961.

³ Hammon, W. McD., and Howitt, B. F., *Am. J. Hyg.*, 1942, **35**, 163.

⁴ Armstrong, C., *Harvey Lectures*, Lancaster, Pa., Science Press, 1941, 39.