The Protective Effect of Irradiation Combined with Sheathing Methods on Experimental Nerve Heterografts: Silastic, Autogenous Veins, and Heterogenous Arteries

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A survey of the literature on the repair of nerve defects in peripheral nerve grafting emphasizes inhibiting the immune response of the host to the graft. Medawar, 33, 34 in 1944 and 1945, stressed the importance of the immune reaction.

Since the first autogenous nerve transplantations on the dog by Phillippeaux and Vulpian in 1870 35 and the first homograft in the human by Albert, in 1878, 1 various techniques have been continued until the present time. Merzbacher, 39 in 1905, made the discrimination between auto- and homografts as opposed to heterografts. Experiments with heterografts have had minimal success over a period of many years. 2, 6, 10, 21, 26, 27, 40, 41, 43, 44 Huber, 24 in 1895, reviewed previous methods employed in the treatment of nerve injuries and described seven methods. In 1942, Young 34 claimed that peripheral nerve segments were the best means of repairing a nerve defect.

Numerous materials have been used for nerve sheathing and tubulation to protect the suture site from cellular invasion and to prevent neuroma formation. In 1882 Vanlair 42 tried decalcified bone as a tube over a 3-cm defect in a dog nerve. This material was also used by Pomerancw 39 in 1900 and by von Auffenberg 2 in 1907.

Büngner 8 in 1891 tried the human brachial artery as a cover for the dog sciatic nerve. Many authors have reported that an artery as a nerve cover gave minimal protection. 4, 5, 10, 13, 19, 22–24, 37, 46 Weiss 50 in 1943 reported the sleeve method of frozen-dried arteries on heterografts and homografts and claimed full functional recovery in cats and monkeys.

The plasma clot technique was used in 1950 by Davis and Ruhe 34 with homografts.

They obtained better results with homografts in the cat sciatic nerve than with the human homograft.

The use of a vein as a sheathing for nerves offered minimal success. 15, 20, 36, 37, 43, 53 Payr 41 in 1900, used magnesium. Many other materials have been tried, most of which induced foreign body reaction with eventual scar contraction and scanty axonal regeneration.

Spurling, 42 in 1943, was the first to cover the suture line with tantalum foil, but found that foil was too brittle. Weiss 21 in 1944, stated that elastic cuffs of tantalum were promising for maximal nerve regeneration, and White and Hamlin, 52 in 1945, obtained less tissue reaction around the sutures and prevented neuroma formation by use of tantalum sleeves.

More recently the successful use of cellulose-acetate filters (Millipore) around the graft has been reported. 12, 13 The Millipore filters not only provided diffusion of extracellular fluid for the regenerating axons, but also acted as a barricade to inflammatory cells. The Millipore filter, however, had disadvantages because of the difficulty of handling and of fragmentation.

Kline, 29 in 1964, stated that the nerve wrapped with processed bovine flexor tendon collagen produces less axon disorganization at the suture line and that axonal carry-through was more orderly in chimpanzees whose nerve had been cut and sutured. He suggested, however, that the processed collagen could stimulate an acute hypersensitive or immune mechanism.

The silicones, which are chemically stable and nontoxic in the body, have been adapted for medical use as injectable subcutaneous and cutaneous prostheses. Clinically, a number of their applications have been tried with wide acceptance in plastic surgery 47 and in neurosurgery 48.
The use of cathode irradiation on homologous and heterologous nerve grafts has been observed to reduce the foreign body reaction and to sterilize the grafts. The irradiated human homograft used in two human cases in repair of both median and ulnar nerve with a 3-inch and 5-inch defect revealed progressive return of sensation in these regions.

Since cathode irradiation on both nerve heterografts and homografts in this laboratory has given encouraging results, it was decided to determine if the immune reaction could be further suppressed by combining irradiated heterografts with different sheathing methods. Irradiated heterografts were covered with Silastic using the plasma clot molding method, with frozen irradiated heterogenous arteries and with fresh autogenous veins, using the sleeve splicing and tubulation methods.

Materials and Methods

This project was designed to study the efficacy of Silastics applied around the suture site or over the graft in protecting irradiated nerve heterografts from fibroblastic invasion. Silastic No. 382 and No. 5392, both medical grade elastomers, were supplied by viscous fluids from the Dow Corning Company. After the addition of the proper amount of catalyst (stannous octoate), the silicone became rubber within a few minutes.

Preliminary experiments were made to evaluate the characteristics of Silastic which would be suitable for our purpose. When Silastic containing methylene blue dye was placed over the suture lines to estimate stablility as a coating, there was no seepage into the suture lines.

Since the coagulation time of Silastic depended on the amount of catalyst used and the concentrated catalyst was said to be an irritant to surrounding tissue, the next step was to investigate the tissue reaction to various concentrations of the catalyst in each type of Silastic. It was established that the least irritable concentration was less than 4% by weight in the fluid Silastic. We found Silastic No. 5392 to be somewhat friable but it did not produce tissue reaction. Silastic No. 382 occasionally produced a tissue reaction by mechanical irritation. We decided to use both kinds of Silastic for covering nerve grafts.

A preliminary study was made to learn if the length of the sheath would affect the blood supply in the nerve graft. The upper facial nerves of 12 rats were cut, sutured with two 7-0 silk sutures, and coated with "Silastic sheathing," 5, 8, 10, and 15 mm in length (Fig. 1 A). The lower facial nerves, which were cut and sutured only, served as a control. After 4 months the nerves were explored (Fig. 1 B), electric action potential was measured, and histological examination was made. The condition of individual groups of fibers in a nerve are to some extent detectable from measurements of summed action potential heights and conduction velocities. With a 5-mm sheath, excellent axonal growth with a good blood supply was found. These findings were confirmed by action potential study (Fig. 1 C and D). The other sizes of Silastic sheaths were unsatisfactory, as compared to the controls, with the graft showing necrosis or disconnection.

The grafts used for these experiments were obtained from fresh human cadavers and freshly sacrificed dogs under conditions as aseptic as possible and immediately packaged in heat-sealed polyethylene bags and frozen to −12°F. Portions of the grafts were maintained in the frozen state and irradiated with 2,000,000 rep by Van de Graaff generator, which sterilized the graft and altered its antigenicity. The grafts were then stored in a freezer at −12°F until used.

Experiment 1. The purpose of our first experiment was to determine the soft tissue reaction to Silastic-coated, irradiated and nonirradiated, subcutaneous implants in rats and to compare histologically the reactions of irradiated and nonirradiated nerves sealed in the Silastic.

Sixty adult rats (Sprague-Dawley) were divided into three groups. Previously prepared nerves were cut into 1-cm segments to serve as implants. The rats were anesthetized with ether, and a subcutaneous 2.5 cm incision was made in each posterior quadrant of the back. The right quadrant, in all groups, served as a control for the same implant without Silastic coating. Group 1 con-