An Experimental Evaluation of the Effect of a Plastic Adhesive, Methyl 2-Cyanoacrylate,* on Neural Tissue

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During the last several years, surgeons have demonstrated a good deal of interest in a new adhesive, methyl 2-cyanoacrylate (Eastman 910 adhesive). This plastic adhesive is a member of the alkyl 2-cyanoacrylate family. It sets rapidly, being polymerized by traces of water, and affords an exceptionally strong bond. Furthermore, the adhesive appears to be self-sterilizin6 and, to date, there have been no reported infections secondary to its use.3,8,9 As a result, many investigators have used methyl 2-cyanoacrylate as a biological adhesive both experimentally and clinically, not only to repair arterial wounds9,7 but to close skin incisions and anastomose bowel9 as well. These reports have stimulated neurosurgeons to use the 910 adhesive. Araki et al.5 coated intracranial aneurysms with the adhesive in animals and in humans. Albin et al.1 have also utilized the adhesive to graft patches of Teflon to dural defects in dogs with good results. Carton and his associates4 recently reported the repair of a tear at the base of an internal carotid aneurysm. The 910 adhesive was used to patch dura mater over the defect; postoperative angiograms demonstrated that the internal carotid artery remained patent.

Several investigators4,8,10 have called attention to an acute inflammatory reaction around arteriotomies closed with 910 adhesive and to thrombosis of vessels whose intima has come in contact with the adhesive. However, in spite of the widespread use of methyl 2-cyanoacrylate, careful adequately controlled evaluations of the effect of this adhesive on tissues other than vessels have not been published. The purpose of this report is to present our experience with implants of methyl 2-cyanoacrylate on canine peripheral nerves and cerebral cortex and on primate optic nerves.

Method†

Two groups of 10 healthy mongrel dogs of both sexes whose weights varied between 30 and 45 lbs. were used. All animals were anesthetized with pentobarbital sodium, 25 mg. per kg. of body weight. Aliquots of 910 adhesive were placed in small sterilized polyethylene bottles before each experiment. Aerobic and anaerobic cultures were taken both at the start and the conclusion of the study (no growth was observed). Strict asepsis was maintained during each operation.

Group I. Peripheral Nerves. The peroneal nerves in both hind limbs were exposed through popliteal incisions while the radial nerves of the forelimbs were exposed by muscle-splitting incisions of the triceps. All nerves were dissected free from their connective-tissue bed and the threshold needed to elicit dorsiflexion was determined using a Grass S-6 stimulator. The peroneal and radial nerves on one side were coated in a circumferential manner over a 3 cm. segment with sterile saline while those on the opposite side were coated over an identical 3 cm. segment with methyl 2-cyanoacrylate using a #2 artist’s brush. All wounds were closed with stainless-steel wire.

At 2, 6, 8 and 12 weeks postoperatively, thresholds of stimulation were determined again and the animals were sacrificed. Both the saline- and the adhesive-coated nerves were removed and fixed in 10 per cent buffered formalin for 1 week. Specimens were then embedded in paraffin and multiple cross and longitudinal sections were made. Sections were stained by hematoxylin and eosin, Masson’s connective-tissue stain, Bodian’s

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† The principles of laboratory animal care as promulgated by the National Society for Medical Research were observed.
method for axons, Morgan's method for myelin, and in some cases Nissl's stain for Schwann cells. Adhesive-coated nerves were then compared with saline-coated nerves from the same animal.

Group II. Brain. The 10 animals in this group were subjected to bilateral occipital trephination. The dura mater immediately beneath each burr-hole was resected, exposing the underlying pia arachnoid and occipital cortex. Five drops of sterile saline were placed on the left cortex while five drops of methyl 2-cyanoacrylate were implanted on the right cortex. Wounds were closed with stainless-steel wire.

The animals were sacrificed with intravenous Nembutal at 2, 6, 8 and 12 weeks postoperatively. All areas suspected of infection were cultured using peptone agar and thioglycollate broth. The dura mater surrounding each burrhole and the entire brain were removed immediately and fixed in 10 per cent buffered formalin for 2 weeks before processing. The stains used were hematoxylin and eosin, Masson, Nissl, Morgan's myelin, and Mallory's phosphotungstic acid hematoxylin.

Results

Group I. Peripheral Nerves. The 10 animals in this group remained well. Examination of gross specimens revealed increased adhesions around adhesive-coated nerves. A light brown discoloration was evident in 10 of the 20 adhesive-coated nerves. Furthermore, thresholds for stimulation were increased in 5 adhesive-coated nerves. The increase in threshold varied between 1 to 6 volts while the thresholds of the control nerves were unchanged. However, serial measurements of limbs failed to reveal any atrophy. The saline-coated control nerves maintained the same threshold and except for a few adhesions at the site of exposure they appeared normal.

Histologic preparations revealed epineurial inflammation, consisting of lymphocytic and plasma-cell infiltrates, increased vascularity and occasional giant cells, in each of the 20 adhesive-coated nerves (Fig. 1). The specimens obtained at 4, 8 and 12 weeks revealed proliferation of connective tissue throughout the epineurial areas of inflammation. In addition, infiltrates of an inflammatory nature involved the perineurium in 17 of the 20 adhesive-coated nerves. In 14 specimens, the epineurial infiltrates extended into nearby fascicles causing tubular and axonal destruction. The specimens obtained at 2 weeks revealed tubular demyelination, axonal fragmentation, and disorganization of fascicles (Figs. 2, 3 and 4). The fascicles damaged were

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**Fig. 1.** Dog U99. Epineurial infiltrate at 2 weeks. Lymphocytes, plasma cells, and occasional giant cells. Hematoxylin and eosin, X496.