Effects of Methyl 2-Cyanoacrylate Adhesives* on the Somatic Vessels and the Central Nervous System of Animals†

D. Yashon, M.D., J. A. Jane, M. C. Gordon, J. L. Hubbard, and O. Sugar

Department of Neurology and Neurosurgery, University of Illinois, College of Medicine, Chicago, Illinois

SYNTHETIC adhesives have been utilized both experimentally and in the correction of certain disorders of the central nervous system. Because of its ease of application and rapid setting, even in a moist environment, methyl 2-cyanoacrylate monomer seemed suitable for clinical trial. To test possible adverse tissue reactions, various sites in experimental animals were exposed to the material. Large vessel reaction was tested on the femoral and carotid arteries. The effect on three compartments of the central nervous system were evaluated: the subdural space overlying the cerebral cortex, the subarachnoid space via the cisterna magna, and the subdural space over the thoracic spinal cord. Eastman 910 monomer and Eastman 910 adhesive gave identical results and will be discussed together.‡ Cats and rabbits were used; no species differences were noted.

Materials and Methods

Forty-seven rabbits and 11 cats were used; half of these were treated with Eastman 910 adhesive and half with Eastman 910 monomer. All surgical procedures were performed using sterile techniques and chlorpromazine-pentobarbital anesthesia.

In 10 rabbits the subdural space was exposed by a large craniectomy and the dura mater excised. The pia-arachnoid over the cerebral cortex was coated with 3 to 6 drops of Eastman 910 adhesive or Eastman 910 monomer which hardened after 1 to 2 minutes. Only the skin was closed. The animals were sacrificed at intervals up to 6 months.

In 11 cats and 2 rabbits, 0.5 cc. of Eastman 910 monomer or Eastman 910 adhesive was introduced into the cisterna magna after suboccipital percutaneous puncture with a 30 infant spinal needle. The animals died or were sacrificed at intervals of 1 day to 3 months.

A midthoracic laminectomy was performed in 25 rabbits. The dura was widely opened and the cord coated with Eastman 910 monomer. The dura mater was left open and the paraspinal muscle and skin were separately closed with interrupted 4-0 silk sutures. These animals were sacrificed at intervals from 2 days to 6 months.

In 10 rabbits, carotid and femoral vessels were coated with either Eastman 910 monomer, or Eastman 910 adhesive. The average diameter of these vessels was 2–4 mm. These animals were sacrificed after 1 to 6 months.

Frequent observation for neurological deficits was carried out.

At the end of each experiment, the animals were killed by an overdose of nembutal. The brain and spinal cord or carotid and femoral arteries were removed and placed in 10 per cent formalin prior to imbedding. The adhesive material overlying the tissue could be easily cut with the microtome. Hematoxylin-eosin, Kluver’s luxol fast blue, and phospho-tungstic acid-hematoxylin were used for staining.

Results

The plastic material flows readily, and, upon hardening, forms an opaque film which adheres to tissues. After extended survival periods, the coated area appears as a dense fibrous covering. Within a month, a dense membrane forms, adherent to the brain and pia mater. The plastic itself tends to become porous and is penetrated by elements of this membrane, which consists of elongated fibroblasts, collagen, new capillaries, multinucleated giant cells, and at times, a dense round cell infiltration. We found no pathological changes in small pial vessels embedded in the Eastman 910 monomer or Eastman 910 adhesive. Neuronal death and gliosis to a depth of 1–2 mm. was marked in the brain stem following injection into the subarachnoid space of the cisterna magna. Changes in the

Received for publication November 15, 1965.

* Eastman 910 Monomer was supplied by Ethicon Inc.
† Supported by General Research Support Grant #137, United States Public Health Service.
‡ See editorial note on p. 876 for clarification of nomenclature.
leptomeninges and surface of the brain or spinal cord (Figs. 1 and 2) were less pronounced than in the subarachnoid space around the cisterna magna.

Neurological deficits were found in 2 of the experimental groups: 1. animals with Eastman 910 monomer or Eastman 910 adhesive in the cisterna magna frequently showed evidence of damage to brain stem structures; this included hemiparesis and alterations in the level of consciousness. 2. Two animals in which the spinal cord was coated showed weakness of the hind limbs and urinary incontinence immediately on awakening from anesthesia. There were similar major neurological signs in 10 others, 5 to 47 days postoperatively. The late onset of neurological signs did not correlate with damage to neural tissue; the histologic evidence of toxic effect was no more evident in these animals than in the 13 which did not develop neurological deficit. In both instances, we attributed the neurological disorder to neurotoxic effect of the adhesives. No neurological deficits appeared after application to the pia-arachnoid of the cerebrum.

When Eastman 910 monomer or Eastman 910 adhesive was applied to the femoral or carotid artery, erosion of the adventitia and media was frequent (Fig. 3). The adhesives gave the same results in these areas. Aneurysmal dilation and arterial thrombosis were not seen. The plastic remained adherent to the adventitia but later became more and more infiltrated with reactive membrane, in a manner comparable to that described in the central nervous system.

The toxic effects of cyanoacrylate adhesives were local and did not damage any tissue more than 2 mm. from the site of application. This is probably due to the rapid setting since there were no differences in basic histologic appearance that correlated with the length of survival time.