Experimental Evaluation of Four Synthetic Adhesives for Possible Treatment of Aneurysms*†

SHYAM B. YODH, M.B., B.S., AND R. LEWIS WRIGHT, M.D.

Neurosurgical Service, Massachusetts General Hospital, and the Department of Surgery, Harvard Medical School, Boston, Massachusetts

REINFORCEMENT of intracranial aneurysms with synthetic agents is relatively recent.1–3,4,6,9,13,23–26 Preliminary experimental evaluation of these agents has been of short duration and on extracranial arteries in animals.5,6,8,10,16,17,19,21,22,24,26–25 Studies of their effects on neural structures, both intracranial and extracranial, have been scant.6,7,11,13,14,29

We are reporting a study of four synthetic agents implanted intracranially in 12 cats and 23 rabbits and their effects on 1) the optic nerve, 2) the orbital surface of the frontal lobe, 3) the dura, and 4) the blood vessels. Two of these agents, M2C-1 (Eastman 910 monomer clinical grade) and EDH-adhesive (Biobond),‡ have been studied experimentally and used clinically by others. Two new agents, Ioplex and Aron Alpha A “Sankyo,”§ have not been studied for intracranial use.

Materials and Method

Materials. The chemical compositions of the four agents are listed below.

1. M2C-1 Eastman 910 monomer (clinical grade). This compound (herein referred to as M2C-1) is composed of stabilized methyl 2-cyanoacrylate monomer.

2. EDH-adhesive (Biobond). This agent (herein referred to as EDH-adhesive) is made up of 6 parts Eastman 910 adhesive (methyl 2-cyanoacrylate monomer modiﬁed with the plasticizer sebocate), a thickening agent (methacrylate), and an inhibitor (SO2); plus 3 parts polyisocyanate (Desmodur-T); plus 6 parts nitrile rubber in a nitromethane solution (Hycar No. 1041).

3. Ioplex. This is a polyelectrolyte complex of polyvinyl alcohol NaSS polysodium styrene sulphonate, combined with polyacrylamide (polyvinylbenzene trimethylammonium chloride) in a 10% NaBr/Dioxane/H2O solvent system.

4. Aron Alpha A “Sankyo.” This agent (herein referred to as AAS) is 98% alpha ethyl cyanoacrylate plus a thickening agent inhibitor 2% without plasticizer.

Operative Technique. Twelve cats (average weight 3.5 kg) and 23 rabbits (average weight 2.0 kg) were used. The cats were anesthetized with intraperitoneal pentobarbital Na 3.6 mgm/kg and the rabbits with intramuscular chlorpromazine 15 mgm/kg plus intravenous pentobarbital Na 2.4 mgm/kg. Sterile operative technique was used throughout the procedure. After local infiltration of the scalp with 1.5 ml of 2% procaine, a right frontotemporal craniectomy (2 cm in diameter) was performed. A dural flap with a temporal base was reflected. Since the animal was in a supine position with the head elevated, drainage of cerebrospinal fluid made it possible to expose the right optic nerve and part of the left with gentle retraction of the right frontal lobe. Two drops of saline were placed on the left optic nerve and allowed to run onto the undersurface of the left frontal lobe. One drop of the adhesive was carefully placed on the lateral aspect of the right optic nerve and the undersurface of the right frontal lobe. In some animals, a thin film was placed...
on the exposed right frontoparietal cortex. The dural flap was replaced, left unsutured, and the skin closed with continuous 3-zero chromic catgut. All animals received intramuscular injections of 600,000 units of benzathine penicillin at the end of the procedure. In postoperative follow-up the animals were watched for any neurological deficit daily for 1 week, then weekly for 1 month, and subsequently at monthly intervals.

Pathological Examination. The animals were sacrificed with an overdose of pentobarbital at intervals of 3, 6, and 12 months. The whole brain was removed with the dura in place and fixed in 10% formalin for 1 week. After gross inspection and palpation, it was cut into 10μ serial sections, each of which included portions of the adhesive, optic nerves, adjoining dura, and orbital surface of the frontal lobes. These sections were stained with haematoxylin-eosin and Woelke's myelin stain.

Results

The general findings were: 1) there was no clinically detectable neurological deficit in any of the animals; 2) the control (left) optic nerve, dura, and orbital cortex were essentially normal; 3) the pial and larger vessels of the anterior cerebral group were patent, even though many of them were surrounded by varying degrees of fibrosis and chronic inflammatory cells; 4) abscess formation was not seen; and 5) there was no species difference noted.

M2C-1. In four rabbits studied, one sacrificed at 3 months and three at 6 months, no plastic could be seen. The area of implantation showed marked adhesions between irregularly thickened dura and cortex. The outer 1 to 2 mm of the right orbital cortex showed marked infiltration with macrophages and areas of necrosis (Fig. 1). The right optic nerve showed marginal demyelination and marked fibrosis that was pulling the nerve to one side. No plastic was seen microscopically, and the nerve itself was not infiltrated with inflammatory cells.

Previous animal studies have shown that M2C-1 disintegrates within the body and completely disappears in from 70 to 90 days; it causes gross and histological damage to the optic chiasm and to the surfaces of the brain and spinal cord; and that it destroys neurons and causes gliosis with cellular infiltration to a depth of 2 mm on the surface of the brain and spinal cord. The results of our study are in agreement with those reported.

Human studies of its intracranial use have reported late thrombosis in man and fatal rerupture within 3 days. In our hospital, there have been three cases of rerupture when this agent was used with fine mesh gauze wrapping on intracranial aneurysms. However, Carton, et al., have reported good results with intracranial use of this agent. An explanation for these conflicting results may be related to the amount of the agent used. At least one firm conclusion can be made: M2C-1 (Eastman 910 monomer clini-