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P H Pevsner, P Klara, J Doppman, E George and M Girton

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Ethyl Alcohol: Experimental Agent for Interventional Therapy of Neurovascular Lesions

Paul H. Pevsner,[1] Peter Klara,[2] John Doppman,[3] Eugene George,[2] and Mary Girton[3]

Perfusion of absolute ethyl alcohol into the middle cerebral artery of six rhesus monkeys was performed using the Pevsner miniballoon catheter system. The animals were sacrificed by thoracotomy and intracardiac perfusion of a mixed aldehyde solution for fixation. Preliminary angiography and electron microscopy suggest absolute ethyl alcohol is a good neurovascular occlusive agent, and a possible replacement for isobutyl 2-cyanoacrylate in the treatment of angiomas and tumors.

The experimental basis of ethyl alcohol vascular ablation in the peripheral vasculature was established in mongrel dogs [1–3]. Clinical experience with this technique has been reported [4]. The organs perfused were kidneys and vascular tumors [4, 5] (M. Huggins, unpublished data). Extensive clinical experience in head, neck, and peripheral vascular lesions using the Pevsner miniballoon system and isobutyl 2-cyanoacrylate was described previously by the authors [6, 7].

This study was initiated to examine the safety and efficacy of ethyl alcohol as a neurovascular occlusive agent for treatment of angiomas and tumors. The Pevsner miniballoon system allows delivery of isobutyl 2-cyanoacrylate into the interstices of the lesion; however, the miniballoon catheter must be quickly removed after injection of isobutyl 2-cyanoacrylate to prevent intravascular fixation of the balloon. This greatly limits superselective angiography through the miniballoon catheter after injection of the occlusive agent. The characteristics of an ideal vascular occlusive agent have been reviewed in a previous report [8], and include availability, ease of sterilization, low viscosity (centipoise < 1), and nonadhesiveness (to prevent intravascular fixation of the miniballoon catheter).

Recent communications of experimental and clinical results using ethyl alcohol suggest it would be an ideal occlusive agent in the cerebral vasculature. This report describes preliminary clinical, angiographic, and electron microscope findings in rhesus monkeys, and supports a role for ethyl alcohol in treatment of cerebrovascular lesions.

Materials and Methods

Six 6–10 kg rhesus monkeys were used. Intravenous sodium pentobarbital (Richmond Veterinary Supply, Richmond, VA) 2 mg/kg was injected for general anesthesia. A 5 French polyethylene catheter was passed into the right or left femoral artery, an internal carotid artery selectively catheterized, and an angiogram obtained (fig. 1A). A new, more flexible version of the Pevsner miniballoon catheter system was placed through the 5 French catheter into the distal opercular branch of the middle cerebral artery (fig. 1B). The distal tip was then pulled back to the proximal middle cerebral artery. Ether-dried absolute ethyl alcohol 0.2 ml was injected through the miniballoon catheter. The catheter was flushed with 0.2 ml normal saline, and then with 0.4 ml Conray 60 (Mallinckrodt, St. Louis). The flush clears the miniballoon catheter of alcohol to prevent precipitation of contrast media in the catheter. This was repeated after additional absolute ethyl alcohol injections of 0.3 ml, 1.0 ml, and 1.0 ml. Angiograms after perfusion with 0.5 ml and 2.5 ml of absolute ethyl alcohol are shown in figures 1C and 1D.

All animals were sacrificed by thoracotomy and cardiac perfusion of a mixed aldehyde solution for fixation. The perfused vessels and contiguous brain were examined with the electron microscope.

Results

No seizures or deaths were observed from the alcohol injections. Early in the study, over 300 ml of saline flush was infused during catheter placement, which resulted in two deaths from pulmonary edema. Careful monitoring of flush solution volumes prevented this complication in the last four animals. The pulmonary edema was clearly due to fluid overload and not a postalcohol injection, central nervous system mediated phenomenon.

Additional animals have been perfused with alcohol but not sacrificed. They are being followed with computed tomography (CT) and will be sacrificed after stabilization of CT findings, according to the schedule described previously [9].

Discussion

Absolute ethyl alcohol appears to meet all the criteria for an ideal vascular occlusive agent. No obvious clinical evidence of toxicity was observed. Ultrastructure electron micrographs revealed thrombus formation in the main middle cerebral artery and contiguous branches; however, the thrombus only filled the proximal part of the vessel within 2 cm of the distal tip of the miniballoon catheter. Beyond this point there was no thrombus, the endothelium was normal, and there was no evidence of endothelial damage in the

[1] Department of Radiology and USUHS, Walter Reed Army Medical Center, Washington, DC 20012. Address reprint requests to P.H. Pevsner, 2524 Virginia Avenue NW, Washington, DC 20037.
[2] Neurosurgery Service, Walter Reed Army Medical Center, Washington, DC 20012.
[3] Department of Radiology, National Institutes of Health, Bethesda, MD 20205.

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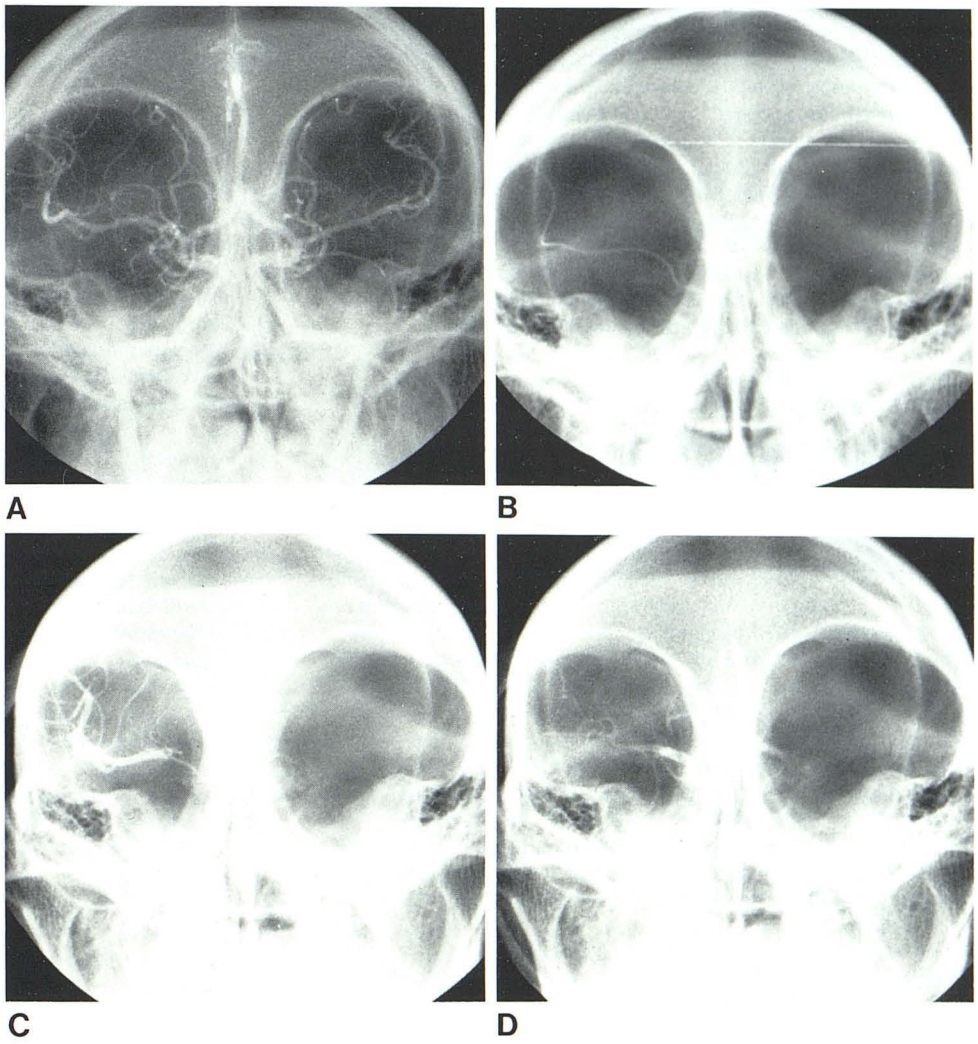

Fig. 1.—Representative angiograms of significant stages of study. **A**, Normal anteroposterior carotid angiogram. **B**, Balloon catheter in distal opercular branch of middle cerebral artery. **C**, Superselective angiogram of middle cerebral artery, postinjection of 0.5 ml ethyl alcohol. Artery remains patent. **D**, Superselective angiogram of middle cerebral artery, postinjection of 2.5 ml ethyl alcohol. Note occlusion.

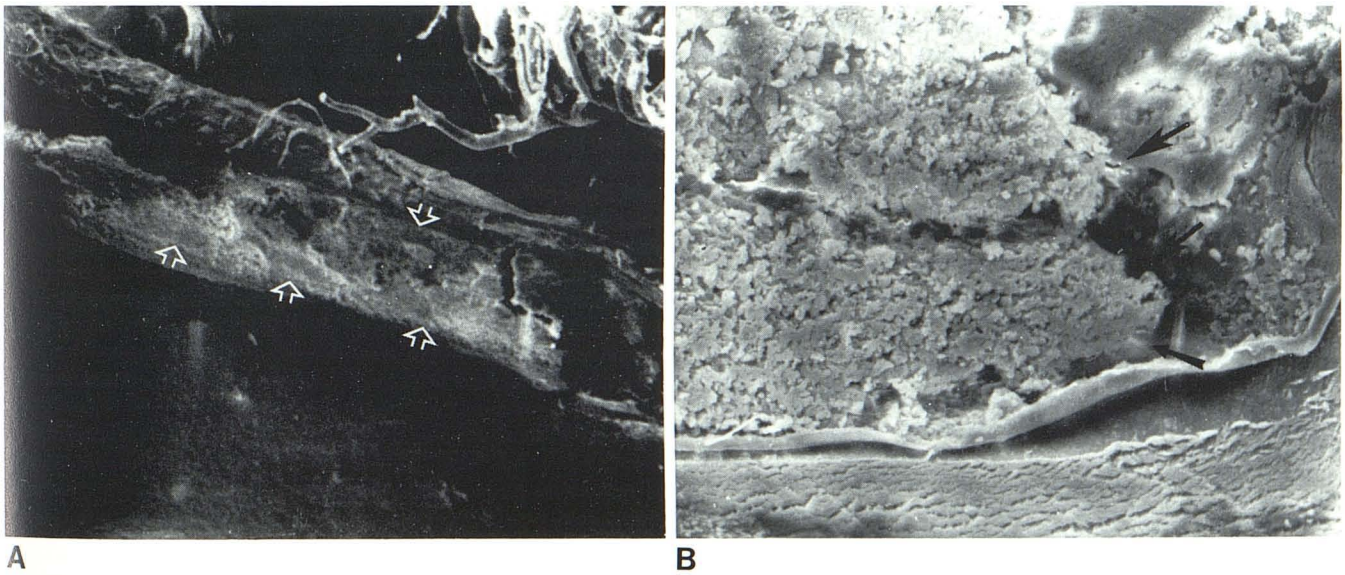

Fig. 2.—Ultraselective electron micrographs of middle cerebral artery thrombus. **A**, Thrombus formation in artery and contiguous branches (*arrows*). **B**, Distal end of thrombus (*arrows*). Note normal epithelium.

more distal vessels (fig. 2). This is in contradistinction to the findings of Buchta et al. [3] who demonstrated parenchymal pathologic changes in similarly perfused canine kidneys. Ultrastructure electron micrographs revealed glomerular basement membrane splitting and degeneration, with necrosis of endothelial, epithelial, and mesangial cells, and loss of structure within the nucleus, mitochondria, endoplasmic reticulum, golgi apparatus, lysosomes, and cytosol. This is probably explained by the large injection rate (2 ml/sec) and volume (0.2 ml/kg) they used. Our volumes were at most 0.1 ml/kg injected at less than one-third the rate.

Preliminary results suggest ethyl alcohol is a good cerebrovascular occlusive substance. Final recommendation for human use awaits further studies on chronic animal preparations.

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