WORK IN PROGRESS

Instant Selective Arterial Occlusion with Isobutyl 2-Cyanoacrylate[1]

Charles T. Dotter, M.D., Martin L. Goldman, M.D., and Josef Rösch, M.D.

Isobutyl 2-cyanoacrylate (IBC) delivered selectively in small doses produced immediate occlusion of the injected arteries in dogs without significant undesired sequelae. In one patient, pelvic hemorrhage was promptly stopped by a similar technique. In another patient, who was on chronic renal dialysis and judged too ill for nephrectomy, IBC occluded both renal arteries and terminated a life-threatening renal protein loss.

INDEX TERMS: Catheters and Catheterization • Embolism, therapeutic • Isobutyl 2-Cyanoacrylate • Kidneys, failure • Pelvis, hemorrhage

Radiology 114:227–230, January 1975

Isobutyl 2-cyanoacrylate monomer (IBC) is a fast-acting liquid adhesive which may be used in place of a suture or as a topical hemostatic agent. A small amount administered intra-arterially produces immediate occlusion of the injected segment. Zanetti and Sherman (1) and others (2, 3) in the U. S. and, more widely, abroad have used it therapeutically to occlude intracranial aneurysms, arteriovenous malformations, and the blood supply of certain types of tumors. This is a preliminary report on our experimental use of catheter-delivered IBC to achieve superselective arterial occlusion in dogs as well as to stop exsanguination from a pelvic tumor in one desperately ill patient and accomplish needed "medical nephrectomy" in another.

EXPERIMENTAL STUDIES

Eleven IBC-induced visceral arterial occlusions were produced in 7 dogs. The left gastric artery was occluded in 5 dogs, the gastroduodenal artery in 3, the inferior pancreaticoduodenal artery in 1, and branches of the superior mesenteric artery in 1. Selective catheterization with a 6.7 French polyethylene catheter was followed by control angiography and superselective catheterization using a siliconized 3 French polyethylene inner coaxial catheter advanced to a point about 2 cm beyond the outer catheter. After the location of the small coaxial catheter had been established by repeat angiography, its lumen was flushed with 5% dextrose in water and a total of 0.3 ml of IBC[2] made radiopaque by the addition of powdered tantalum[3] was injected over a period of about two seconds. When the lumen of the inner catheter became occluded, it was immediately removed and the outer catheter withdrawn about 1 cm to maintain its luminal patency and intra-arterial freedom and permit angiographic documentation of the occlusion. A typical occlusion is shown in Figure 1.

Two dogs with 0.5-ml IBC occlusions of the gastroduodenal arteries died of autopsy-proved duodenal infarction, perforation, and ischemic pancreatitis within three days. One of these dogs also had IBC-induced occlusion of the inferior pancreaticoduodenal artery. Selective left gastric artery occlusion caused no apparent ill effects in the other 5 dogs. Follow-up angiograms taken one month later showed no

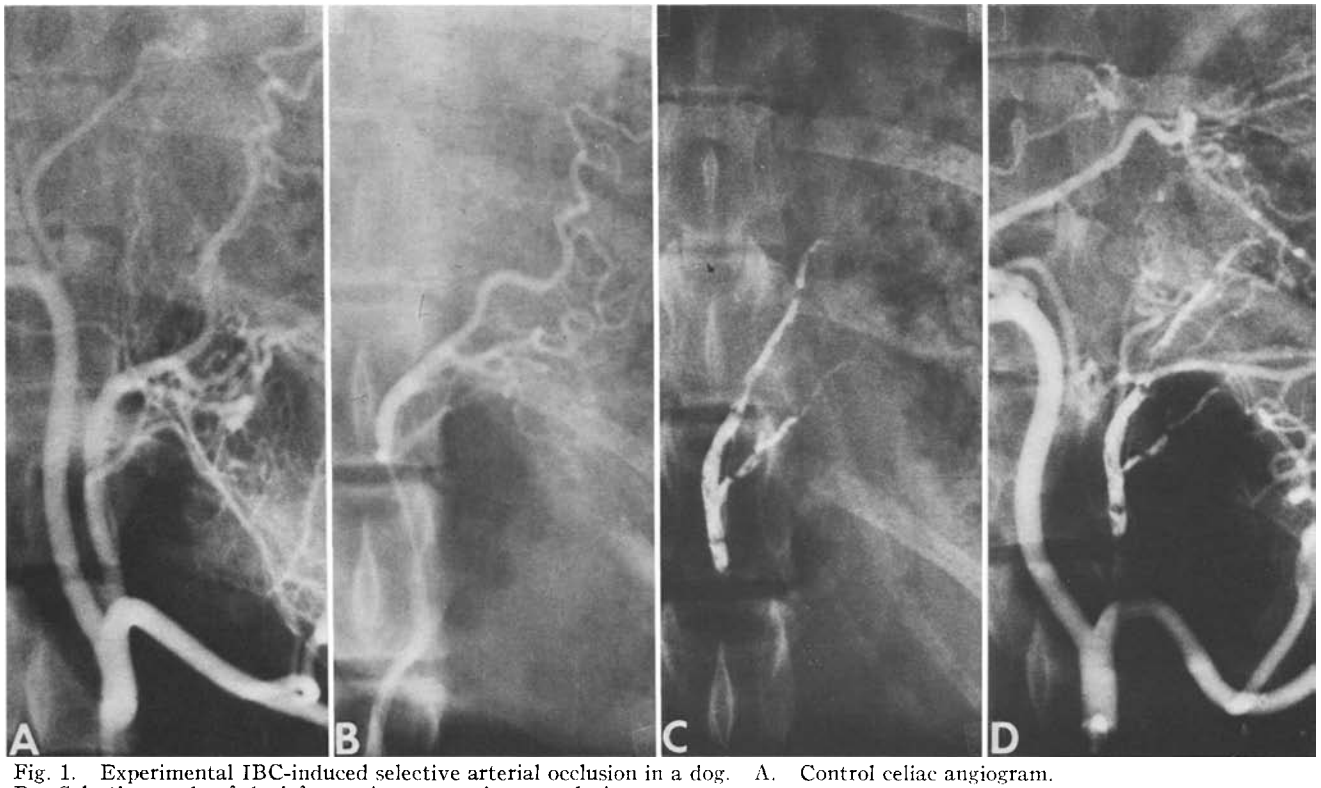

Fig. 1. Experimental IBC-induced selective arterial occlusion in a dog. A. Control celiac angiogram.
B. Selective study of the left gastric artery prior to occlusion.
C. Bucrylate–tantalum bolus in the left gastric artery.
D. Celiac angiogram taken two weeks later shows persisting left gastric artery occlusion and the development of collaterals.

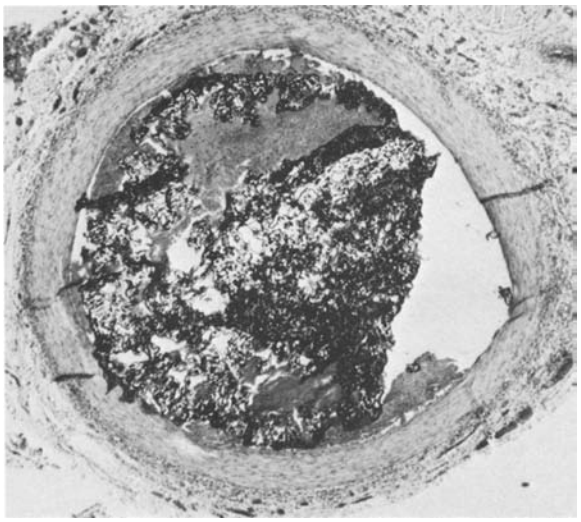

Fig. 2. Experimental IBC occlusion of the left gastric artery in a dog. Cross section of the left gastric artery a month after occlusion shows an organized intraluminal plug composed of IBC/tantalum and clot. (H & E, 30×)

change in the appearance or extent of the occlusions. All animals were sacrificed and anatomical studies made. Histological sections through the occluded segments revealed that the IBC was contained entirely within the lumen of the vessel, intermixed with partially organized blood clots (Fig. 2). Most occluded vessels exhibited a mild fibroblastic inflammatory reaction extrinsic to the muscularis. Two of the 11 occluded vessels had focal areas of inflammation with partial replacement of the media. In one early experiment, a 0.5-second injection of IBC caused separate embolization of distal arterial branches as small as 30 μ; and in one of the dogs that died, IBC was found in duodenal veins measuring 200 μ. When 0.3 ml was administered over a period of two seconds, the IBC remained as a single bolus, filling only those arterial segments immediately distal to the injection site.

CASE REPORTS

CASE I: Emergency selective arteriography in a 38-year-old woman with massive vaginal bleeding due to pelvic carcinomatosis showed gross extravasation from an eroded, tumor-encased right hypogastric artery (Fig. 3, A). She had received 21 units over the preceding three days because of continuing hemorrhage and shock—14 units in an outlying

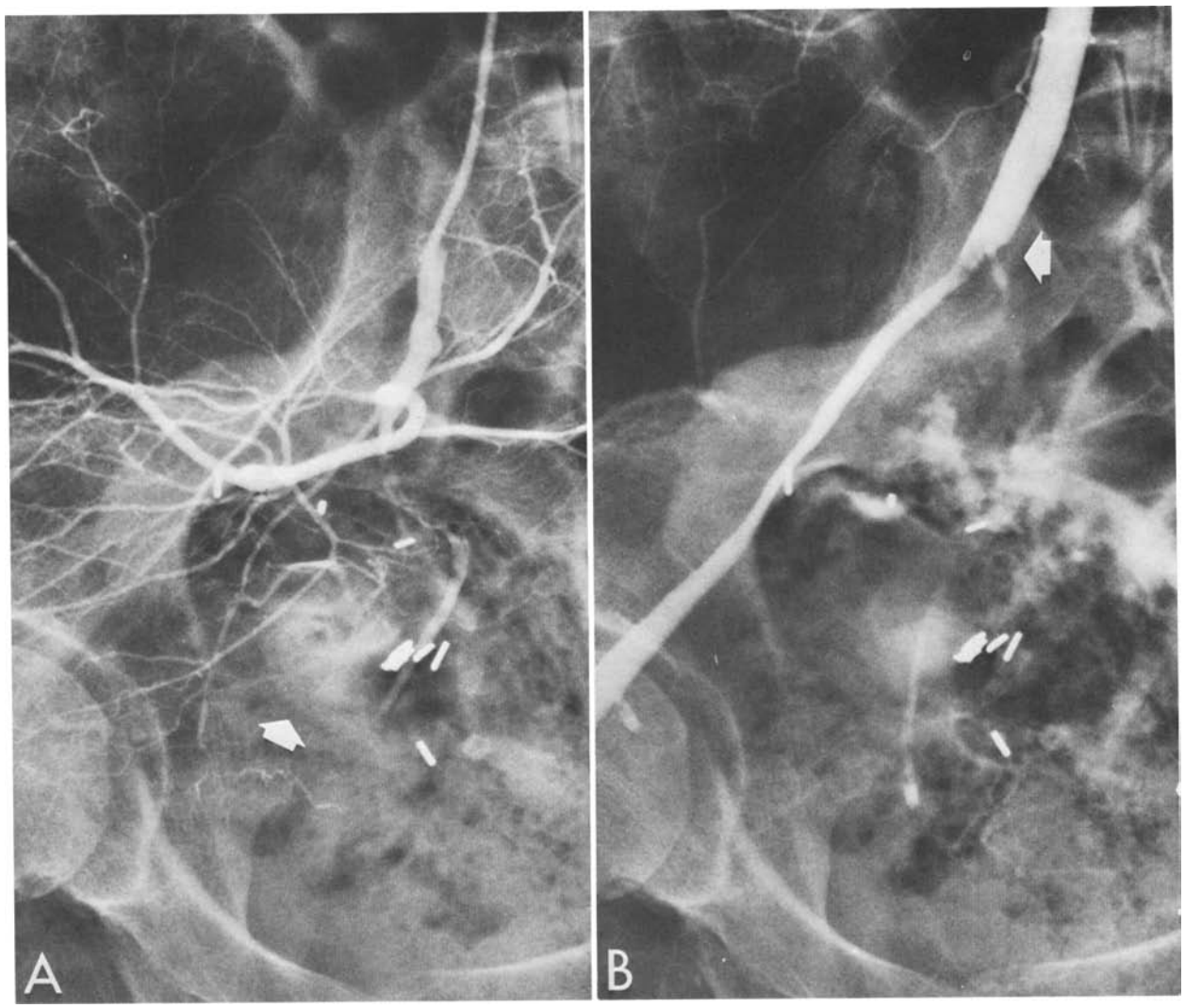

Fig. 3. Therapeutic occlusion in a 38-year-old woman with gross bleeding from a pelvic carcinoma. A. Selective hypogastric arteriogram shows neoplastic invasion with gross extravasation of contrast material (arrow).
B. Common iliac arteriogram taken four minutes after IBC occlusion of the hypogastric artery (at arrow). The contrast agent diffusely infiltrating the tumor is from the earlier study. The external iliac artery is narrowed due to tumor encasement.

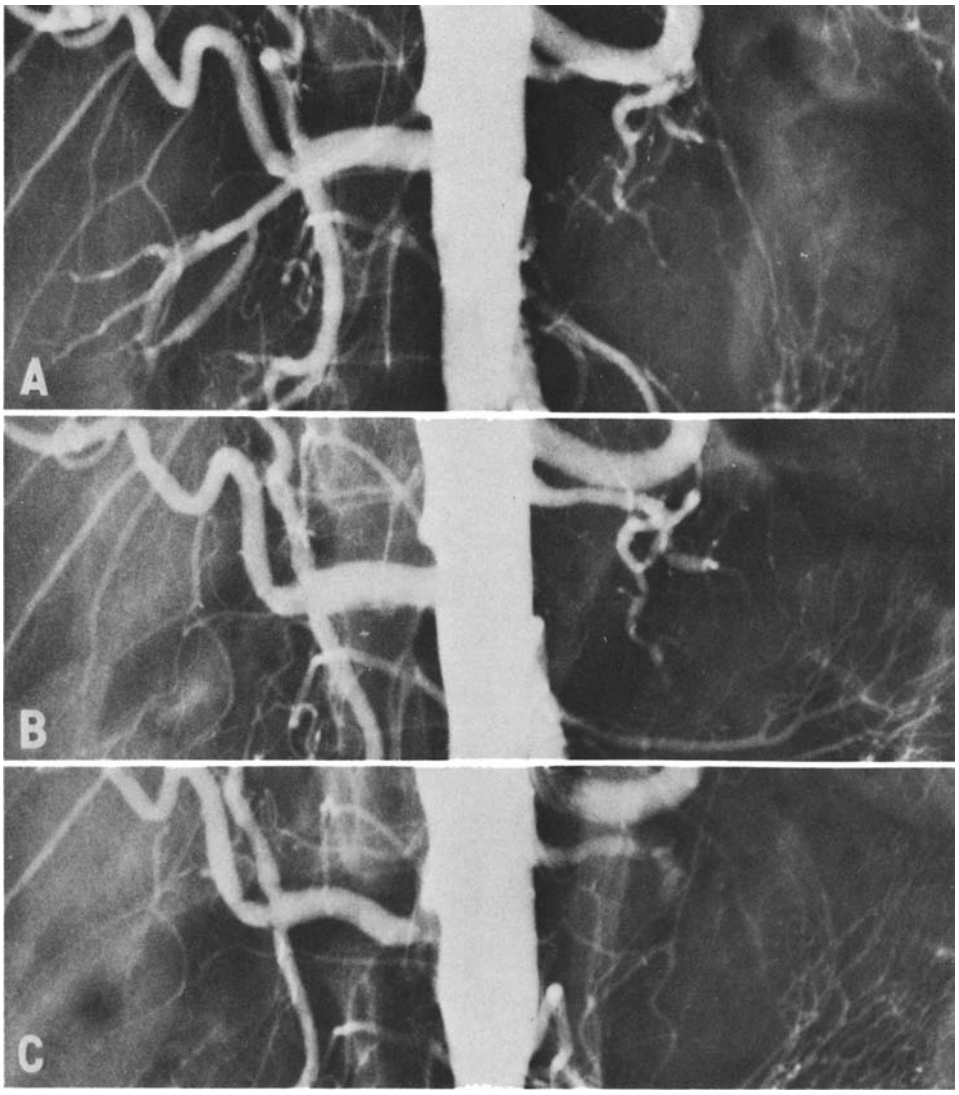

Fig. 4. Bilateral therapeutic renal artery occlusion in a 35-year-old woman with glomerulonephritis and chronic renal failure who was judged to be too ill for nephrectomy. A. Control angiogram shows two small renal arteries.
B. Angiogram taken after IBC occlusion of the right renal artery.
C. Angiogram taken after occlusion of the left renal artery. The clinical course thereafter was benign and the patient survived.

hospital and 7 units on the day she arrived at our hospital—and it was felt that she would not survive an attempt at surgical ligation of the tumor-encased bleeder.

Informed consent was obtained, and in an effort to save the patient's life a 3 French polyethylene catheter was passed to a point 1 cm beyond the tip of the diagnostic catheter and 0.9 ml of IBC was injected in about one second. The inner catheter was immediately removed, the diagnostic catheter was withdrawn into the common iliac artery, and angiography was repeated. Although some contrast material had extravasated into the tumor, a large filling defect was already present in the hypogastric artery. A second arteriogram obtained four minutes later showed complete occlusion of the hypogastric artery (Fig. 3, B) without further angiographic or subsequent clinical evidence of bleeding. The patient died of advanced tumor three days later, and autopsy showed complete occlusion of the artery by polymerized IBC and associated thrombus proximal to the site at which it was broken down by the tumor. Although her life could not be saved, it was at least possible to prevent her from bleeding to death, while her family was spared an even larger debt to the blood bank and a costly, potentially lethal attempt at surgical ligation was avoided.

CASE II: A 35-year-old woman with a chronic six-year history of renal failure due to membranous glomerulonephritis had been maintained on intermittent hemodialysis for two years. Because of severe renal protein loss and consequent difficulties in maintaining the dialysis shunt, bilateral nephrectomy was scheduled but had to be canceled following a cerebrovascular accident. She was referred to the radiology department for a "medical nephrectomy," *i.e.*, permanent bilateral selective renal artery occlusion. Informed consent was obtained, and 0.8 ml of IBC was injected into the right renal artery in one second *via* a 6 French catheter, producing immediate occlusion. Two days later the left renal artery was occluded in a similar fashion (Fig. 4). Although there was no pain or fever following occlusion, moderate leukocytosis and a mild elevation in diastolic blood pressure occurred but were readily controlled by Apresoline (Ciba). Since her occlusions

a month ago, the patient has remained anuric and her protein loss has stopped. She is being maintained on dialysis pending possible renal transplantation.

DISCUSSION

In many reported cases, serious episodes of arterial and capillary bleeding have been controlled by selective injection of vasospastic agents (4, 5) and temporary occlusion has been achieved by balloon catheters (6–8). Several selective catheter techniques have been used to produce permanent occlusion, including but not limited to the use of autologous clots (9), Gelfoam (10, 11), and Ivalon (12). Autologous clots do not readily form in patients with coagulopathies such as those which often underlie or contribute to the severity and difficulty of treating such bleeding. Furthermore, thromboembolic occlusions are susceptible to lytic recanalization, which is not always desirable. Fragments of Gelfoam are difficult to work with and require a catheter with a lumen much larger than that needed for injecting fluid IBC. As a consequence, the selectivity of Gelfoam is less than that of IBC, and one is more likely to hit undesired targets. To date, the FDA has not approved the clinical intra-arterial use of IBC. A request for federal authorization to use it as an investigational new drug is pending.

While the effectiveness of IBC in producing permanent arterial occlusion has been established and its minimal reactivity documented (3), its long-term effects within the human body require further investigation. As illustrated in 2 of our dogs, it can kill if injected into a region where the resulting infarct is lethal; however, as shown in our 2 patients, it can also save the patient's life.

ACKNOWLEDGMENT: We wish to thank Fansteel Metals, North Chicago, Ill., for providing the powdered tantalum without charge.

REFERENCES

1. Zanetti PH, Sherman FE: Experimental evaluation of a tissue adhesive as an agent for the treatment of aneurysms and arteriovenous anomalies. J Neurosurg **36**:72–79, Jan 1972
2. Sashin D, Goldman RL, Zanetti P, et al: Electronic radiography in stereotaxic thrombosis of intracranial aneurysms and catheter embolization of cerebral arteriovenous malformations. Radiology **105**:359–363, Nov 1972
3. Matsumoto T: Tissue Adhesives in Surgery. Flushing, N. Y., Medical Examination Publ. Co., 1972
4. Rösch J, Dotter CT, Antonovic R: Selective vasoconstrictor infusion in the management of arterio-capillary gastrointestinal hemorrhage. Am J Roentgenol **116**:279–288, Oct 1972
5. Baum S, Nusbaum M: The control of gastrointestinal hemorrhage by selective mesenteric arterial infusion of vasopressin. Radiology **98**:497–505, Mar 1971
6. Dotter CT, Lukas DS: Acute cor pulmonale. An experimental study utilizing a special cardiac catheter. Am J Physiol **164**:254–262, Jan 1951
7. Wholey MH, Stockdale R, Hung TK: A percutaneous balloon catheter for the immediate control of hemorrhage. Radiology **95**:65–71, Apr 1970
8. Dotter CT, Rösch J, Lakin PC, et al: Injectable flow-guided coaxial catheters for selective angiography and controlled vascular occlusion. Radiology **104**:421–423, Aug 1972
9. Rösch J, Dotter CT, Brown MJ: Selective arterial embolization. A new method for control of acute gastrointestinal bleeding. Radiology **102**:303–306, Feb 1972
10. Margolies MN, Ring EJ, Waltman AC, et al: Arteriography in the management of hemorrhage from pelvic fractures. N Engl J Med **287**:317–321, 17 Aug 1972
11. Bookstein JJ, Goldstein HM: Successful management of postbiopsy arteriovenous fistula with selective arterial embolization. Radiology **109**:535–536, Dec 1973
12. Porstmann W, Wierny L, Warnke H, et al: Catheter closure of patent ductus arteriosus. 62 cases treated without thoracotomy. Radiol Clin North Am **9**:203–218, Aug 1971

---

[1] From the Department of Diagnostic Radiology, University of Oregon Medical School, Portland, Ore. 97201. Presented at the Work In Progress: Diagnosis session of the Fifty-ninth Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 25–30, 1973.

Supported in part by USPHS grants HL03275 and HL05828, the James Picker Foundation (on the recommendation of the Committee on Radiology, NAS-NRC), and the George Alfred Cook Memorial.

[2] Eastman Chemical Products, Kingsport, Tenn.

[3] Fansteel Metals, North Chicago, Ill. sjh