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New Microballoon Device for Transluminal Angioplasty of Intracranial Arterial Vasospasm

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A new microballoon device has been developed to treat intracranial arterial vasospasm by transluminal angioplasty. The balloon is composed of a unique silicone elastomer that will elongate and conform to the blood vessel lumen, thereby decreasing the risk of vessel rupture. The balloon device, which can be either flow-directed or catheter-guided, is permanently affixed to a 2.0-French microcatheter and introduced from a transfemoral arterial approach. Two balloon sizes are currently available. The smaller-sized balloon, used in most cases, measures 0.85 × 3.50 mm uninflated, will accept a volume of 0.10 ml, and will expand to 3.5 × 12.5 mm. The larger balloon, used in six of 14 cases, measures 1.5 × 3.9 mm uninflated, accepts a volume of 0.50 ml, and expands to 7.5 × 13.5 mm. In clinical trials, this device has been successful in dilating both focal and diffuse areas of vasospasm in multiple territories. Thus far, 40 vascular territories have been successfully treated in 14 patients 15–73 years old. In each case, there was angiographic evidence of successful dilatation, and in 10 patients (71%), clinical improvement in the neurologic condition.

Transluminal angioplasty techniques may be useful for reversing some of the serious neurologic sequelae associated with acute intracranial arterial vasospasm.

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Arterial vasospasm due to subarachnoid hemorrhage is a leading cause of serious morbidity and mortality in patients with ruptured intracranial aneurysms. It is estimated that in the United States, 400,000 people harbor an aneurysm; 28,000 patients present each year with a subarachnoid hemorrhage [1–3]. More than 50% of these patients die or suffer major disability due to hemorrhage, often as a consequence of vasospasm leading to ischemia and stroke [4, 5].

Despite a myriad of pharmacologic agents that have been used to prevent or reverse the severe sequelae of vasospasm, no drug or surgical technique has demonstrated the ability to consistently reverse the serious complications of decreased cerebral perfusion. It is for this reason that we developed a new silicone microballoon device to study the effect that intraluminal angioplasty has on dilating spastic intracerebral blood vessels and reversing the associated neurologic complications of cerebral ischemia.

Materials and Methods

Patients with vasospasm were selected for treatment with transluminal angioplasty if they had one of two indications: (1) acute vasospasm induced during endovascular detachable balloon embolization therapy of an intracranial aneurysm or (2) angiographic evidence of acute severe vasospasm associated with subarachnoid hemorrhage, with resultant neurologic decline and no response to medical and pharmacologic therapy including volume expansion and/or induced hypertension. A CT or MR scan was obtained, if possible, prior to angioplasty to ensure that an infarct in the vascular distribution of spasm had not occurred prior to interventional therapy.

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Forty vascular territories in 14 patients 15–73 years old were treated with this new silicone microballoon device. In the anterior circulation the following vessels were treated: internal carotid artery (nine), middle cerebral artery (nine), and anterior cerebral artery (two). In the posterior circulation the vessels treated included the vertebral artery (five), basilar artery (six), and posterior cerebral artery (nine). Eleven patients (79%) were treated for vasospasm associated with hemorrhage and three patients (21%) were treated for spasm that occurred during intravascular balloon embolization therapy. Nine patients (64%) had diffuse segmental narrowing involving more than one vascular territory. Five patients (36%) had focal narrowing of only one vascular territory.

All procedures were performed in the neurointerventional angiography suite. A transfemoral arterial approach was used under local anesthesia with 1% Xylocaine. Via the Seldinger technique, the femoral artery was punctured with an 18-gauge single-wall needle and a 7.5-French sheath was inserted. A baseline coagulation time was then measured.

The balloon used for percutaneous transluminal angioplasty of spastic intracerebral vessels is manufactured as a custom device to our specifications (Interventional Therapeutics Corp., South San Francisco, CA). It is composed of a unique blend of silicone elastomers that provide enhanced expansion and superior elongation properties while maintaining a soft, low-tension shell (Fig. 1). The nature of the silicone material enables the balloon to minimize the potential damage to the endothelial wall of the blood vessel owing to the ability of the silicone balloon to conform to the surrounding tissues [6–10].

The balloon is available in two different sizes depending on the diameter and anatomic location of the vessel to be treated:

1. The medium-sized balloon measures 1.5 × 3.9 mm, will accept 0.50 ml of volume, and will expand to 7.5 × 13.5 mm. This balloon is used to dilate areas from the petrous to internal carotid artery and the vertebral artery.

2. The smaller-sized balloon measures 0.85 × 3.50 mm uninflated, accepts a volume of 0.10 ml, and will expand to 3.5 × 12.5 mm. The vast majority of patients with intracerebral arterial vasospasm involving the supraclinoid internal carotid artery; anterior, middle, and posterior cerebral arteries; and basilar artery were treated with procedures using this balloon (Fig. 2).

The balloon is chemically affixed to either a 2.0-French polyethylene catheter or the 2.2-French Tracker (Target Therapeutics Corp., San Jose, CA) to prevent detachment. An advantage of the polyethylene catheter is that it can be shaped with steam into a variety of curves, which will facilitate entry into the anterior, middle, or posterior cerebral arteries. The Tracker catheter has a softer, distal 18-cm segment and may be used in conjunction with a 0.016 or 0.014 in. (0.041- or 0.036-cm) steerable guidewire, placed to the catheter tip, to aid in subselecting distal intracerebral vessels. A stainless steel vent tube, 0.010 in. (0.025 cm) in outer diameter, is used to vent air from the delivery catheter and balloon just prior to inflation. Metrizamide, at a concentration of 200 mg I/ml, is used to opacify the balloon and catheter. The balloons and catheters are sterilized by an ethylene oxide gas sterilization process to avoid damage to the silicone elastomer and catheter tubing.

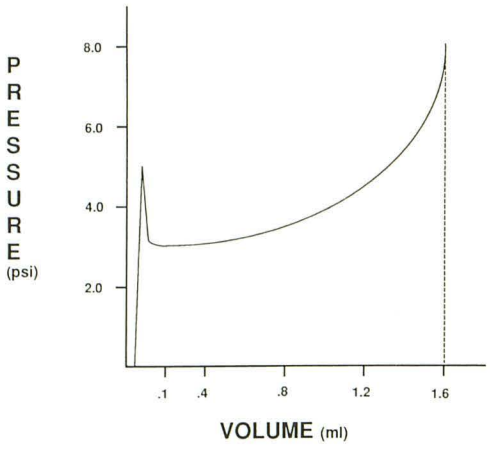

Fig. 1.—Pressure—volume curve shows low-pressure profile of silicone balloon. As balloon is inflated to 0.05 ml, initial yield point is reached. With continued inflation, balloon actually "softens," as depicted by trough between 3.0 and 8.0 psi. At a volume of 1.60 ml, balloon ruptures owing to tearing of silicone shell.

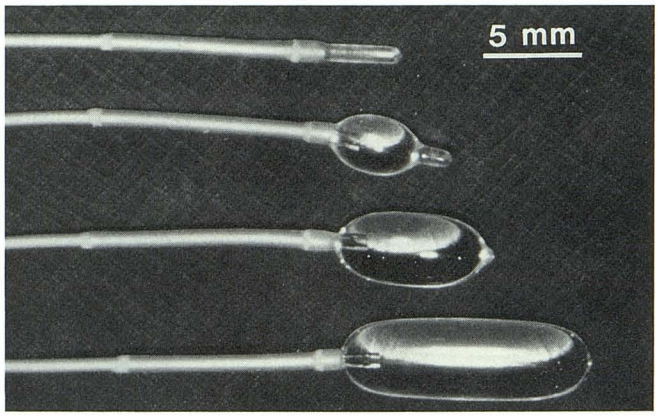

Fig. 2.—Uninflated, partially inflated, and fully inflated angioplasty balloon (*top* to *bottom*, respectively) used for dilating spastic intracerebral vessels. Balloon inflates from proximal to distal, which aids in balloon advancement in diffuse arterial spastic blood vessels.

A 7.3-French nontapered polyethylene catheter is used as the guiding catheter (Cook Corp., Bloomington, IN). It is placed from the femoral artery sheath into the vertebral artery or proximal internal carotid artery, depending on which vascular territory is to be treated. Five thousand units of heparin, for a 70-kg patient, is then given IV for systemic anticoagulation to prevent thrombus formation. The balloon and catheter are introduced through the 7.3-French catheter and the dead space between the two catheters is perfused with heparinized saline. Once the balloon is visualized outside the guiding catheter, it can be safely inflated and advanced to the site of vasospasm by flow direction or by gently advancing the affixed catheter. A digital subtraction "road map" of the intracerebral blood vessels demonstrating the site of spasm can be obtained by contrast injection through the 7.3-French guiding catheter [11].

Angioplasty is then performed by gentle inflation and deflation across the spastic segment(s) under fluoroscopic guidance. A "sausage-shaped" appearance to the balloon is achieved during inflation as the balloon dilates the spastic segment and conforms to the blood vessel lumen. As opposed to angioplasty for atherosclerotic lesions, only minimal pressures (in the range of 1–3 atm) and volumes (0.05–0.50 ml) are required for dilatation of spastic intracerebral blood vessels. Occlusion times are kept under 5 sec during the actual dilatation to minimize further ischemic changes in the distal vascular territory. The progress of the procedure can be easily monitored by digital subtraction angiography performed through the 7.3-French catheter.

Since the procedure is done under local anesthesia, continuous neurologic monitoring can be performed throughout the procedure to assess clinical changes in cerebral perfusion. This technique therefore provides an endovascular angiographically controlled technique to

dilate spastic intracerebral vessels from a transfemoral arterial approach.

Results

In each of the 40 vascular territories treated by balloon angioplasty, we were able to successfully dilate the area of spasm back to normal luminal diameter. There was no evidence of intimal disruption, thrombus formation, dissection, or vessel damage. Angiographically, there was evidence of improved cerebral perfusion. This was documented on angiography immediately after the angioplasty procedure. In six patients who had follow-up angiography several days to 2 weeks after the procedure, there was continued evidence of wide patency of the treated vessel(s). The areas not treated by angioplasty continued to remain in spasm.

Clinically, 11 (79%) of 14 patients showed evidence of neurologic improvement immediately or within 24 hr after the procedure. In five of these cases, there was dramatic improvement, in which the patients went from a comatose or moribund state to being awake and responsive to commands.

In three cases (21%), despite the angiographic success of dilating spastic intracerebral vessels back to normal luminal diameter, there was no clinical improvement. In one of these cases, angioplasty was performed 14 days after the initial subarachnoid hemorrhage, with the patient having been comatose and in grade V neurologic condition for 2 weeks. Despite dilatation of the posterior circulation, there was no clinical improvement and the patient eventually died from sepsis and renal failure. It was believed that this patient had already suffered irreversible brainstem damage prior to the angioplasty procedure. In two other patients in grade V condition and comatose, spasm was treated acutely; however, there was no clinical improvement after the dilatation procedure. It was believed that the angioplasty procedure did not contribute to the patient's eventual demise, but it was also not sufficient to change the clinical situation.

In one case, 24 hr after angioplasty of the middle cerebral artery, a hemorhagic infarct developed in the basal ganglia territory and the patient died. This patient had presented with an acute subarachnoid hemorrhage due to rupture of a distal basilar artery aneurysm. Diffuse spasm of both the posterior and anterior circulation was present and dilatation of the vertebral, basilar, both posterior cerebral, and left middle cerebral arteries was performed successfully. Immediately after the procedure, the patient improved neurologically and was able to respond to commands and move her extremities. However, over the next 24 hr she became moribund and a CT scan demonstrated a large hemorrhage in the left basal ganglia territory.

Angioplasty was performed in three patients for vessel spasm associated with intravascular balloon embolization therapy of an intracranial aneurysm. There was immediate clinical evidence of altered neurologic function, manifested by hemiparesis, lethargy, and aphasia when the spasm was induced. Immediately after angioplasty, there was a return to normal neurologic function with angiographic evidence of restoration of normal cerebral perfusion.

Representative Case Reports

Angioplasty of Posterior Circulation

A 52-year-old man had a subarachnoid hemorrhage from a basilar tip aneurysm (Fig. 3A). Initial neurologic examination revealed the patient to be stuporous with nuchal rigidity and no lateralizing deficits. The patient improved after a ventriculoperitoneal shunt for hydrocephalus. Forty-eight hours after the hemorrhage, he was alert and followed commands with only occasional confusion, in grade 2 condition. However, 24 hr later he became increasingly lethargic and unresponsive, developed pathologic posturing, and became apneic requiring intubation, in grade 4 condition. Despite intense medical management including volume expansion and induced hypertension, the patient continued to decline neurologically.

A second arteriogram demonstrated diffuse vasospasm of the posterior circulation involving the intracranial vertebral arteries, the entire basilar artery, and both posterior cerebral arteries (Fig. 3B). From a transfemoral arterial approach, transluminal angioplasty of the intracerebral vertebral, entire basilar, and both posterior cerebral arteries was performed without complication (Fig. 3C). The follow-up cerebral angiogram demonstrated return to normal luminal diameter in all the territories treated (Fig. 3D).

One hour after the procedure, the patient went from a semicomatose state to a more alert state and was able to follow simple one-stage commands and move all four extremities purposefully. For that reason it was believed the patient should undergo surgical clipping of the aneurysm. Of concern was the potential for rehemorrhage of the aneurysm following dilatation of the spastic arterial segment proximal to the aneurysm. Surgical clipping of the aneurysm was performed without complication, and the follow-up angiogram 2 days later demonstrated wide patency of all the vessels that were successfully dilated. The patient had a prolonged hospital course with intensive neurologic management. On discharge the patient was awake, alert, and oriented with the ability to follow commands, communicate, and move all four extremities. At 23 months of clinical follow-up the patient continues to improve with full cognition, ambulation with a cane, and marked improvement in motor function of both upper and lower extremities.

Angioplasty of Anterior Circulation

A 51-year-old woman presented with a large subarachnoid hemorrhage due to rupture of a distal basilar artery aneurysm (Fig. 4A). She was initially in grade 2 neurologic condition. Six days later she became semicomatose; was paretic, with flexion only to pain in her extremities; and deteriorated to grade 4 condition. An arteriogram demonstrated severe diffuse spasm of the anterior and posterior circulation (Fig. 4B). Initially, angioplasty was performed of the basilar and posterior cerebral arteries; the patient remained in grade 4 condition. Angioplasty was then performed of the left middle cerebral artery territory (Fig. 4C). After this procedure the patient became more responsive and was able to respond to commands and move her lower extremities and left upper extremity. However, she continued to have right arm and face paresis. A CT head scan immediately after the angioplasty procedure demonstrated no evidence of hemorrhage (Fig. 4D). Twenty-four hours later, the patient developed a fixed and dilated left pupil and became unresponsive. A repeat CT head scan demonstrated a large parenchymal hemorrhage involving the left basal ganglia territory and subinsular region (Fig. 4E). The hemorrhage was believed to be secondary to reperfusion of the lenticulostriate arteries in a territory of evolving infarction that was not apparent on the initial CT head scan.

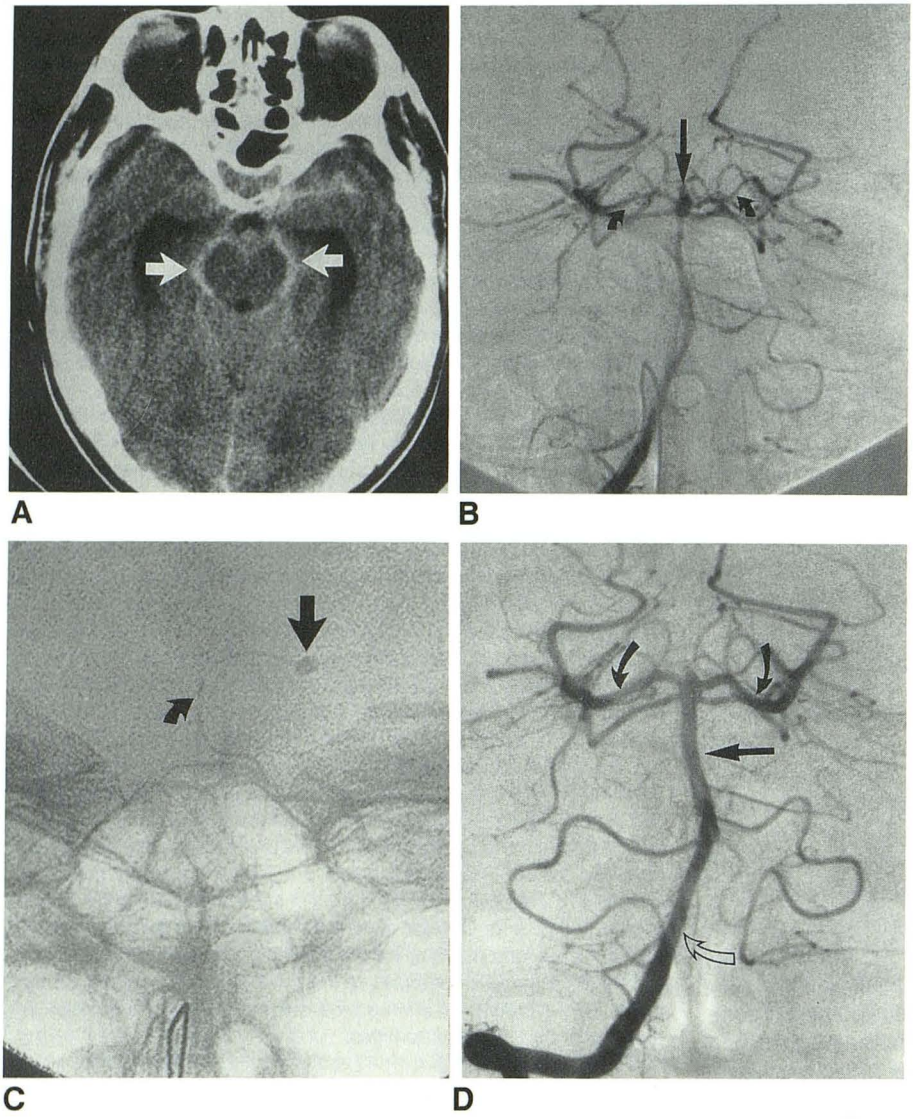

Fig. 3.—*A*, CT scan shows diffuse subarachnoid hemorrhage in basal cisterns due to rupture of distal basilar artery aneurysm (*arrows*).

***B*, Right vertebral angiogram, frontal view, shows distal basilar aneurysm (*straight arrow*) and diffuse spasm of intracerebral portion of vertebral artery, basilar artery, and both posterior cerebral arteries (*curved arrows*).**

***C*, Silicone microballoon in left posterior cerebral artery (*straight arrow*). The 2.0-French polyethylene catheter traversing basilar artery is attached to the balloon (*curved arrow*).**

***D*, After angioplasty of intracerebral vertebral artery (*open arrow*), entire basilar artery (*straight solid arrow*), and both posterior cerebral arteries (*solid curved arrows*), there is return to normal luminal diameter of treated blood vessels.**

Discussion

While the past two decades have witnessed significant improvement in the microneurosurgical treatment of intracranial aneurysms, the morbidity and mortality of subarachnoid hemorrhage remains high. More than half the patients die during the first 3 months. Even among survivors, fully 64% of patients discharged from the hospital never achieve the quality of life they had before the hemorrhage [12, 13].

Little progress has been made in reducing the morbidity and mortality of the initial hemorrhage. There are three major causes of delayed neurologic deficits that may be amenable to therapy: rebleeding, hydrocephalus, and intracranial arterial vasospasm. The associated cerebral ischemia secondary to narrowing of the caliber of major vessels at the base of the brain after aneurysmal subarachnoid hemorrhage is an important and major cause of delayed serious morbidity and mortality. Symptomatic intracranial arterial vasospasm occurs in about 30% of patients who survive the initial hemorrhage; it occurs most often between 3 days and 2 weeks [5, 14].

A large number of pharamacologic agents have been evaluated in the treatment of symptomatic vasospasm in humans and laboratory animals. These have included sympathomimetic amines, adrenergic blocking agents, parasympathomimetic drugs, serotonin antagonists, phosphodiesterase inhibitors, prostaglandins, antiplatelet drugs, local anesthetics, and calcium antagonists. While results in laboratory animals have, on occasion, shown promise, no drug has proved to be entirely effective in preventing or reversing symptomatic vasospasm secondary to subarachnoid hemorrhage. Regimens that focus on increasing cardiac output and lowering blood viscosity have received increasing interest in recent years, but are not consistently of clinical value [15–18].

In 1984, Zubkov et al. [19] reported 33 patients in whom 105 vascular territories were successfully treated by balloon angioplasty using a latex balloon. This report stimulated our group to develop a method to dilate spastic intracerebral vessels by an endovascular technique. We chose silicone over latex balloons because of the inherent softness of the

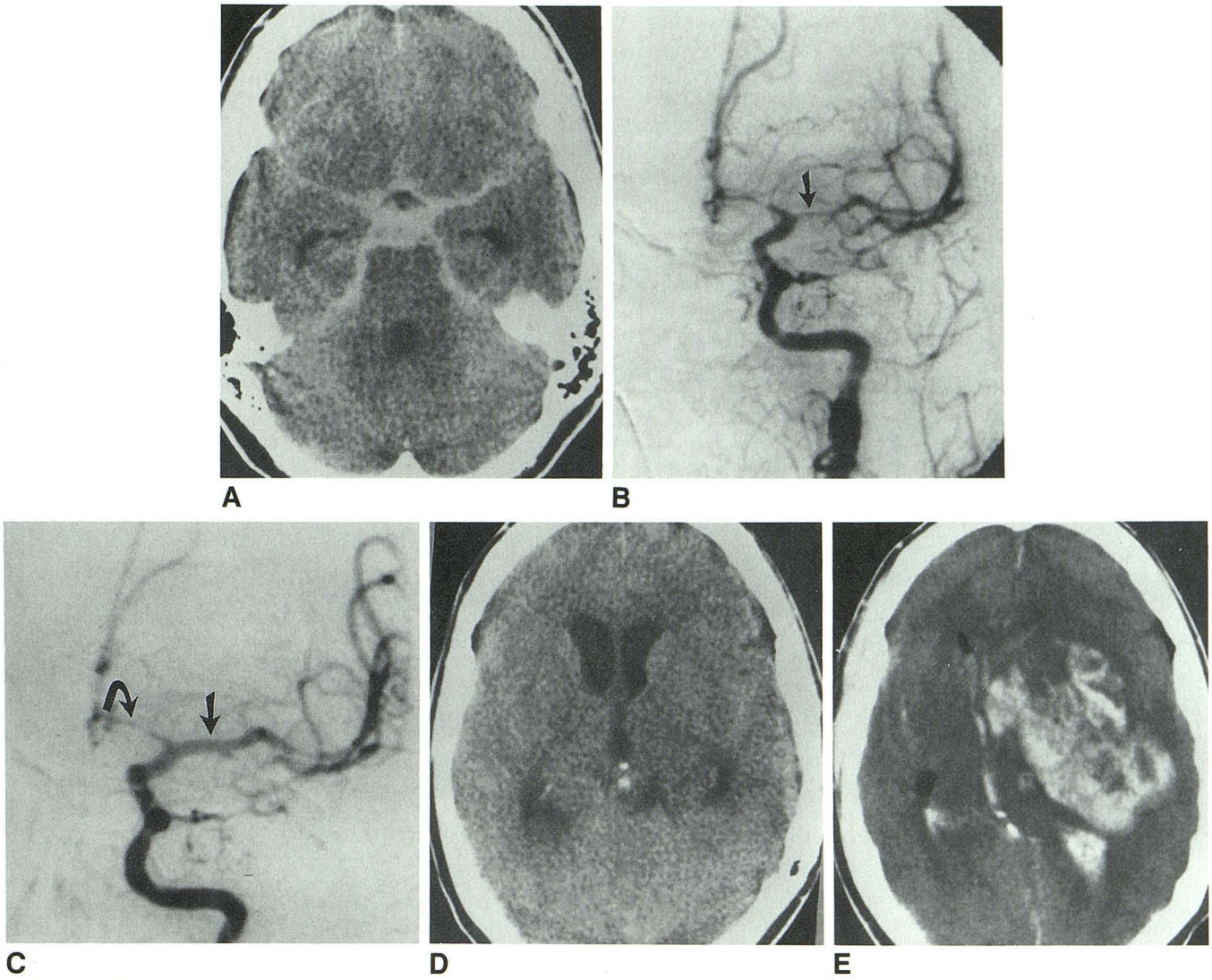

Fig. 4.—*A*, CT head scan shows diffuse blood in subarachnoid cisterns due to rupture of distal basilar artery aneurysm.
***B*, Left internal carotid arteriogram shows spasm of anterior and middle cerebral arteries (*arrow*).**
***C*, After angioplasty of left middle cerebral artery (*straight arrow*), there is return to normal luminal diameter of vessel. Anterior cerebral artery, which was not dilated, remains in spasm (*curved arrow*).**
***D*, CT head scan immediately after angioplasty procedure shows no evidence of hemorrhage.**
***E*, CT head scan 24 hr later shows large parenchymal hemorrhage in left basal ganglia and subinsular region, probably due to reperfusion of lenticulostriate vessels in area of unrecognized prior infarction.**

silicone elastomer. In addition, silicone materials are stable, inert to most substances, and biocompatible with the intravascular system [20–22]. Of the elastomeric family of materials, silicone provides the greatest degree of consistency in response and configuration [8, 9].

The silicone elastomer used to fabricate the angioplasty balloon is blended from several components to provide enhanced expansion and superior elongation properties, with a low tension set. Unless cyclically fatigued, it is highly resistant to tension set and distortion of size or configuration. Silicone is also an ideal material since it can provide a high degree of conformational structure and allows the balloon to be placed in restrained areas with minimal damage to the surrounding vessel walls. The balloon shell possesses isotropic expansion capabilities that will respond with gradual enlargement when inflated with fluid; other materials retain a pressure buildup and then suddenly expand, thus significantly increasing the risk for vessel rupture [22, 23]. In addition, the balloon is mounted on a 2.0-French polyethylene catheter that is steam-formable, thus allowing entry into specific vascular territories such as the anterior or middle cerebral artery. Owing to the inherent ability of silicone to inflate from its proximal to distal end, the balloon can be advanced even with minimal or no flow advantage.

Long-term clinical studies as well as basic science research in animal models is still required to determine the effects of balloon angioplasty for intracranial arterial vasospasm. Balloon angioplasty for vessels narrowed as a result of vaso-

spasm is different from narrowing caused by atherosclerotic disease. Therefore, the histologic changes associated with dilatation of spastic intracerebral vessels are different [24–32]. At least angiographically, there appears to be a restoration to normal luminal diameter without any evidence of intimal injury on immediate or delayed follow-up arteriograms. The effect of angioplasty in relation to cerebral perfusion of the microvasculature still needs to be assessed. However, it is apparent that balloon angioplasty is successful in reversing the acute effects of cerebral ischemia induced by endovascular embolization therapy. It is also apparent that we can reverse the angiographic appearance of focal and diffuse spasm caused by subarachnoid hemorrhage in the major cerebral vessels with improvement of perfusion and reversal of neurologic deficits. We do not know, however, why vasospasm does not recur after angioplasty when blood is still present in the subarachnoid space.

In summary, transluminal angioplasty of spastic intracerebral vessels using this newly developed microballoon device is possible. It may aid in the treatment options for symptomatic patients with cerebral ischemia who are not responsive to conventional medical or pharmacologic therapy.

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