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Embolization of Experimentally Created Aneurysms with Intravascular Stent Devices

Glen Geremia, Michael Haklin, and Luke Brennecke

PURPOSE: To assess the effectiveness of self-expanding, cobalt-alloy stents in the treatment of aneurysms in a canine model and to observe the pattern of blood flow and formation of fibrotic scar tissue. **METHODS:** Porous metallic stents were endovascularly placed across the necks of experimentally created side aneurysms in the carotid arteries of three dogs; aneurysms were also created in the opposite carotid arteries in these animals to serve as controls. **RESULTS:** Before stent placement, angiography of the carotid arteries demonstrated whirl-like, vortex flow of blood within the lumens of the aneurysms. Inflow was seen along the distal aneurysm wall; outflow was demonstrated along the proximal wall; slower vortex flow was present in the central lumen. Immediately after stent placement there was disruption of the usual vortex flow with stasis of contrast media and blood within the lumen. Inflow and outflow patterns were no longer seen. Complete ablation of these aneurysms was evident at follow-up angiographic studies—1 week, 1 month, and 2 months after stent placement. The stented carotid arteries remained widely patent; control aneurysms and carotid arteries were patent and unchanged. Histopathologic analysis revealed fibrotic reactive scar tissue completely filling the stented aneurysm pouches. **CONCLUSION:** Treatment of selected intracranial aneurysms via an endovascular approach has merit and could supplant more invasive, risky, and costly surgical procedures in some cases.

Index terms: Aneurysm, embolization; Arteries, carotid; Interventional instrumentation, stents; Interventional neuroradiology, experimental; Animal studies

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Current treatment of most intracranial aneurysms is surgical, requiring general anesthesia and craniotomies, but the efficacy of nonsurgical, endovascular approaches is being assessed in the treatment of specific types of aneurysms (1–4). Endovascular techniques entail either packing the aneurysm lumen, for example with balloons or metal coils, or completely occluding the native vessel that harbors the aneurysm. Potential complications of these procedures include: (*a*) aneurysm rupture caused by injury of the fragile aneurysm wall while packing the lumen with balloons or coils; and (*b*) immediate or delayed ischemic changes after occlusion of the native vessel that harbors an aneurysm.

The purpose of this study was to test the effectiveness of endovascular stents in the treatment of side aneurysms created in mongrel dogs. Changing blood flow dynamics within an aneurysm can promote thrombus formation (5), and the flow patterns demonstrated in these experimentally created lateral aneurysms coincided with the experience of previous authors confronting the same types of aneurysms (6–8). The stent does not enter the aneurysm lumen and thus lessens the possibility of wall rupture. Its weaved wire mesh, which interferes with the usual blood flow patterns, promotes the formation of thrombus and, eventually, organized fibrosis within the aneurysm.

Materials and Methods

Experimental aneurysms were created in three mongrel dogs, each weighing about 25 kg; our protocol was approved by the Institutional Animal Care and Use Commit-

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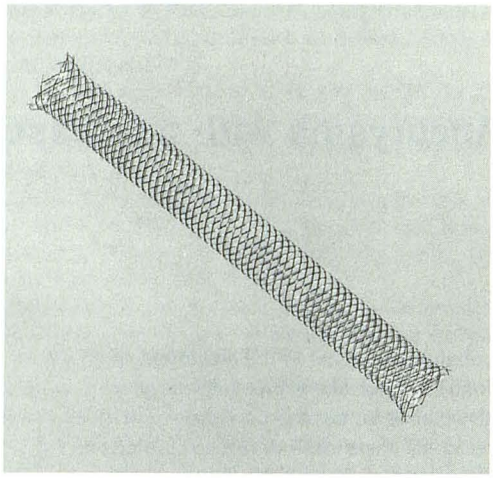


Fig 1. Unconstrained, self-expanding metal porous stent (Schneider) measuring 5 mm in diameter by 40 mm in length.

tee of Rush-Presbyterian-St Luke's Medical Center. The surgical technique and patency rate in this model have been previously reported (9).

Two aneurysms placed in tandem and measuring 1.0 × 0.5 cm and 1.5 × 0.5 cm were created along the length of each carotid artery (four aneurysms in each dog). The aneurysm pouches were made by using the adjacent jugular vein. The two aneurysms in a single carotid artery occupied no more than a 2-cm segment of the vessel. After aneurysm creation, the dogs were allowed to heal for 1 week before carotid angiographic studies, performed via the transfemoral artery approach to demonstrate the created aneurysms. A single, self-expanding stent (Schneider, Minneapolis, Minn) mounted on a 7-F catheter was placed endovascularly within the carotid artery across the neck of each aneurysm (Fig 1). The stents are made of a cobalt alloy and measure 4.0 cm in length by 0.5 cm in diameter. The opposite carotid artery with its two aneurysms remained as the control. Angiography was performed on each carotid artery before and immediately after stent placement. Follow-up angiography was performed at 1 week, 4 weeks, and 8 weeks after stent placement. The stented and control carotid arteries (and aneurysms) were resected for histopathologic study after the final angiographic study.

Results

Initial angiographic studies demonstrated patency of all carotid arteries and aneurysms in all dogs (Fig 2). Characteristic vortex flow patterns were identified in the aneurysm pouches. Inflow occurred along the distal aneurysm wall; outflow was identified along the proximal aneurysm wall; slower vortex flow was present within the central aneurysm lumen. Immediately after stent placement, stasis of contrast medium and blood was seen in the aneurysm pouches within the stented carotid segment on angiography (Fig 3). Ablation of these aneurysms with carotid artery patency was noted angiographically 1 week later and throughout the study (Fig 4). The stented carotid arteries remained patent. The control carotid arteries and aneurysms were patent and unchanged. Histopathologic analysis revealed fibrotic reactive tissue completely filling the stented aneurysm pouches (Figs 5 and 6). Neointima surrounded the stent wires along the inner lumen of the carotid artery, and the elastic lamina was outwardly compressed by the stent wires (Figs 7 and 8).

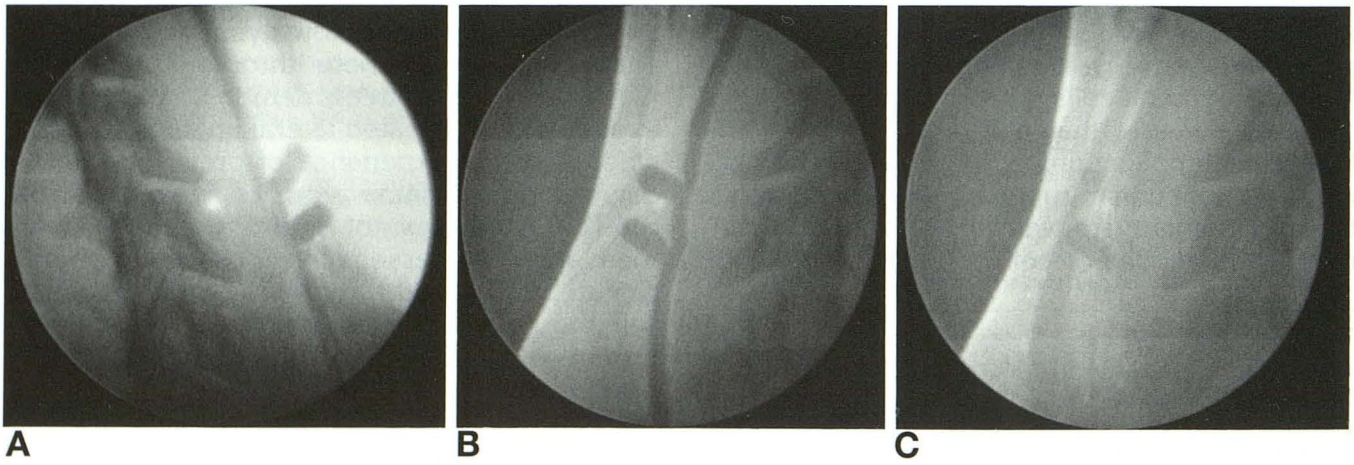


Fig 2. Initial angiogram obtained 2 weeks after aneurysm creation.
A, Left carotid artery as control. The carotid artery and aneurysms are widely patent.
B, Right carotid artery before stent placement. The carotid artery and aneurysms seem to be widely patent in this early image.
C, A later image shows rapid washout of contrast medium.

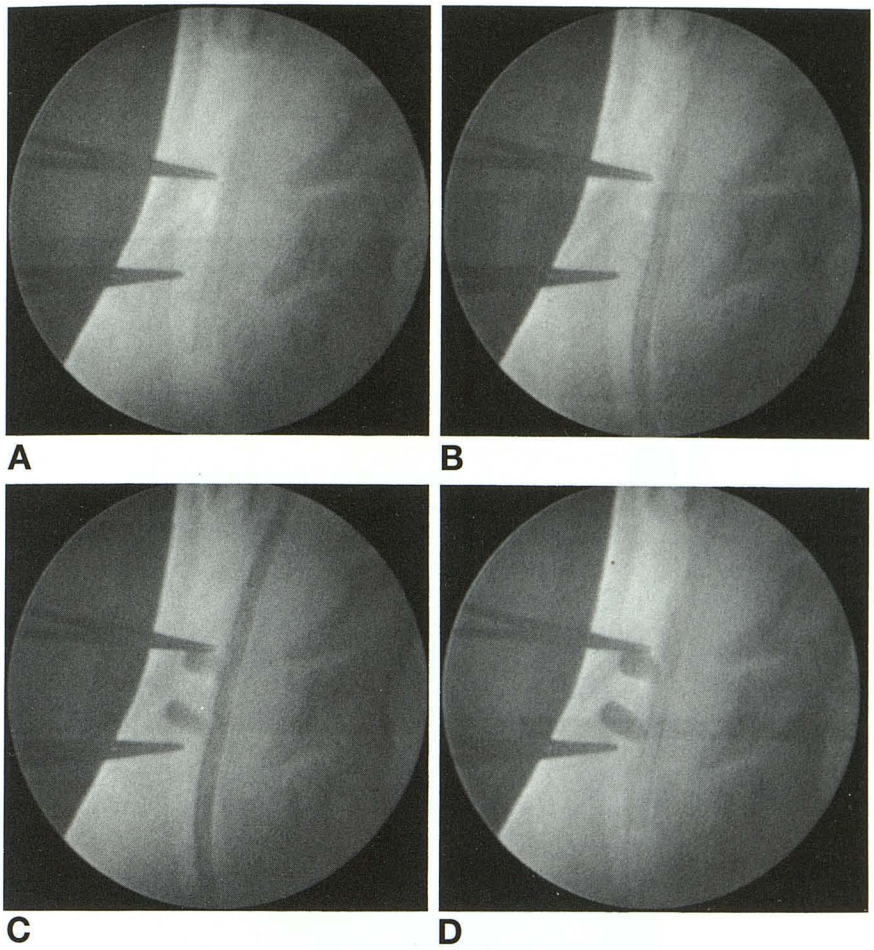


Fig 3. Angiogram of right carotid immediately after stent placement.

A, Hemostats point to metallic stent within the carotid artery.

B, After contrast infusion there is delayed filling of the aneurysm pouches.

C, Contrast eventually fills the aneurysms.

D, A later image shows stasis and delayed washout of contrast.

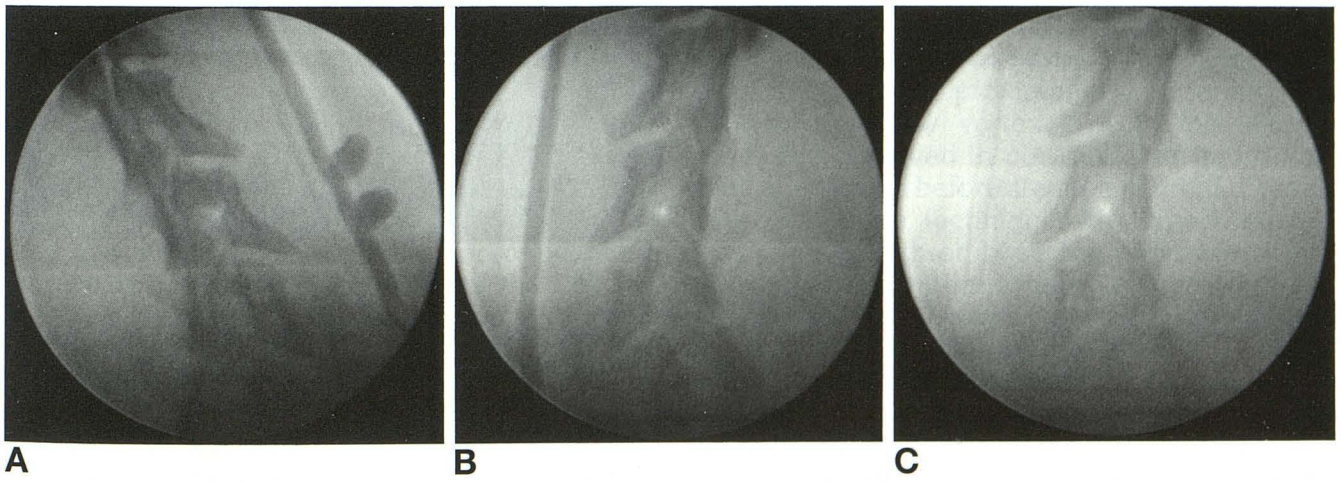
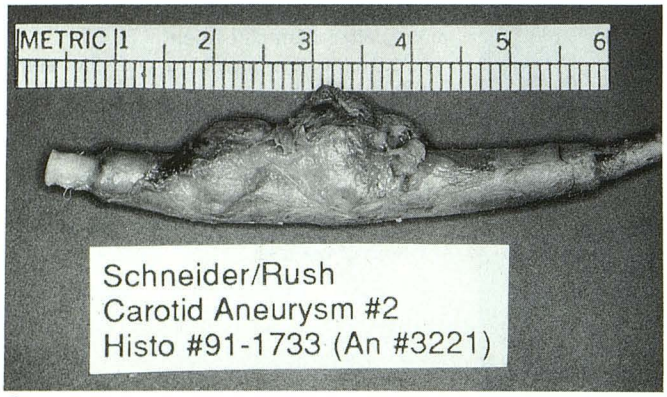


Fig 4. Eight weeks after placement of stent.

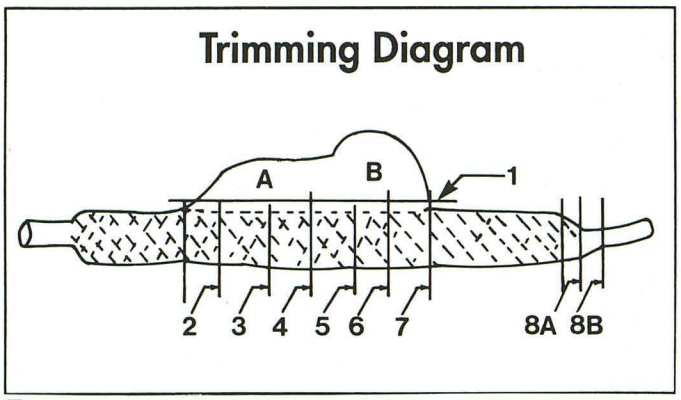
A, Control left carotid artery and its aneurysms are widely patent.

B, Right carotid artery is widely patent, and previously seen aneurysms are ablated.

C, A later image shows no delayed filling of the aneurysms. The stent is visible and unchanged in its location.



A



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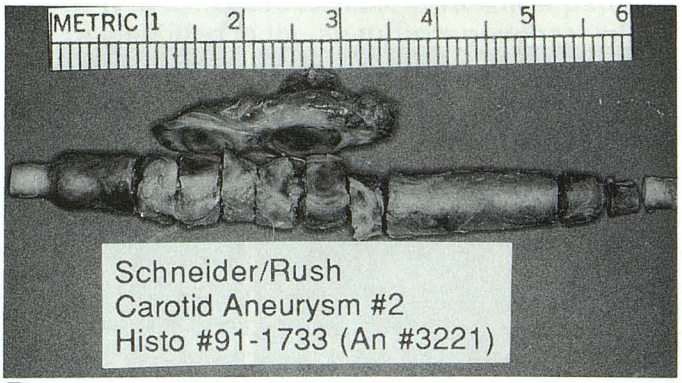

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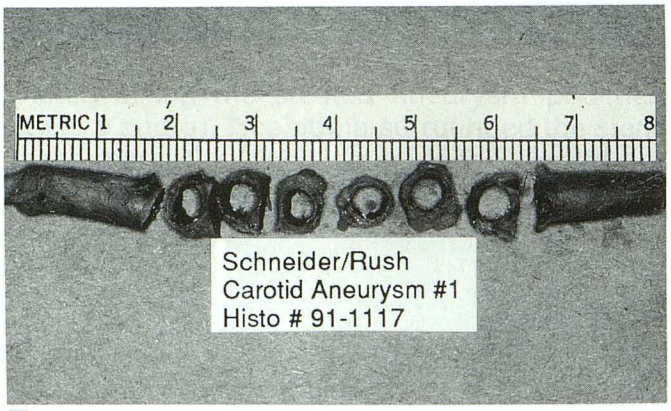

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Fig 5. Gross specimen of carotid artery segment containing stent and aneurysms (refer to trimming diagram).

A, Gross uncut specimen.

B, Trimming diagram.

C, Cut 1 through the bases of the aneurysms reveals dense fibrous tissue within each aneurysm lumen.

D, Cross-section through the carotid artery containing a stent at the level of aneurysms bases.

E, Cross-sections through the carotid artery reveal wide patency.

Discussion

Endovascular techniques for aneurysm therapy have evolved during the last 20 to 25 years. The largest reported series of aneurysms treated endovascularly is by Romodanov and Shcheglov from the Kiev Institute of Neurosurgery (10). In 1989, Shcheglov described 617 cases treated with latex balloons (Shcheglov VI, Endovascular Occlusion of Saccular Intracranial Aneurysms: Results in 617 Patients, presented at the 27th Annual Meeting of the American Society of Neuroradiology, Orlando, Fla, March 19–24, 1989). He succeeded in occluding aneurysms while preserving the parent arteries in 91% of cases; in the remaining 9%, the parent vessel was sacrificed to treat the aneurysm.

Higashida et al in 1991 reported their results in 215 cases of intracranial aneurysms treated with detachable balloons (2). Primary occlusion occurred in 88 aneurysms (40.9%), with preservation of the parent vessels.

Fox et al reported their results in 65 patients with surgically unclippable aneurysms treated

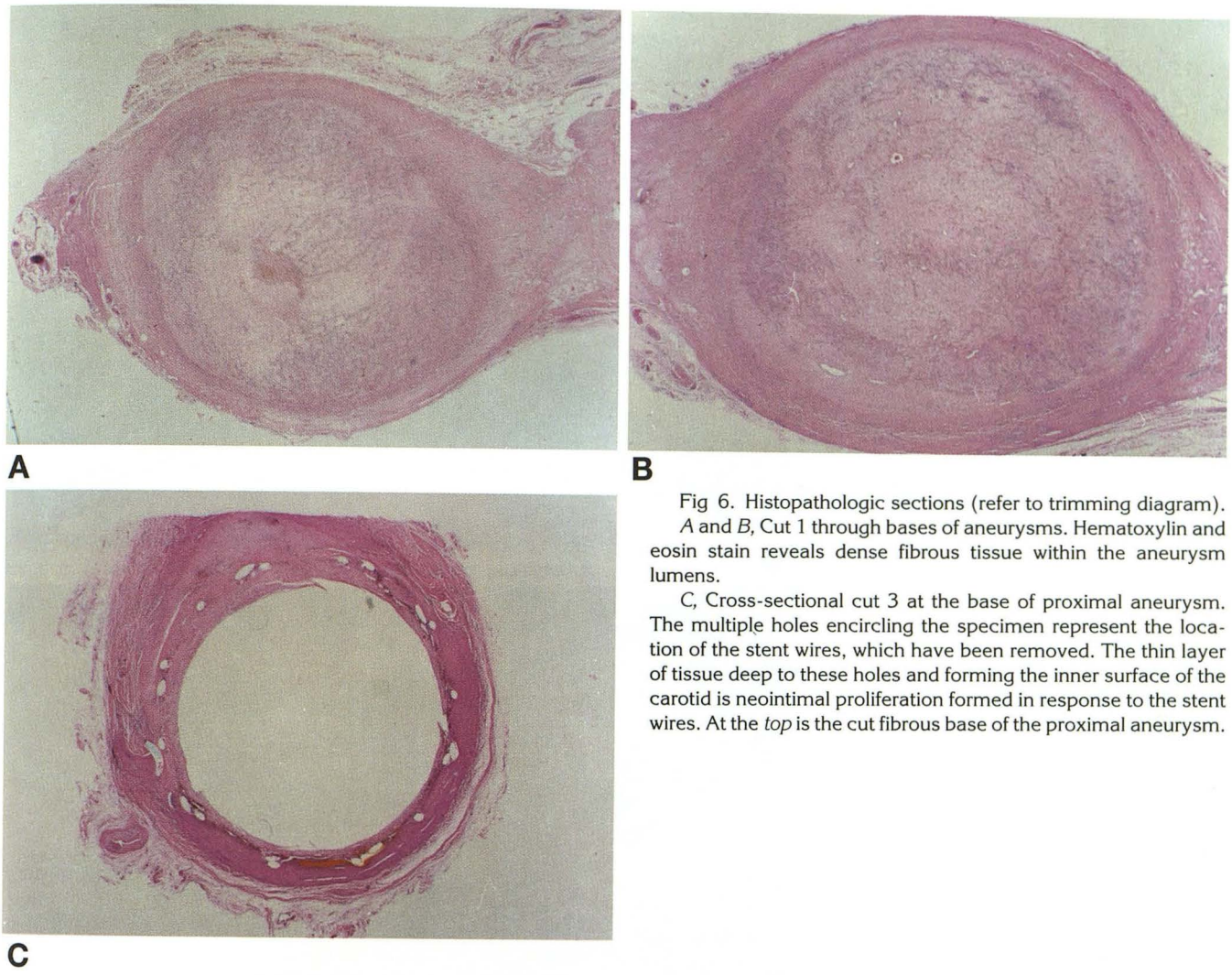

Fig 6. Histopathologic sections (refer to trimming diagram).

A and *B*, Cut 1 through bases of aneurysms. Hematoxylin and eosin stain reveals dense fibrous tissue within the aneurysm lumens.

C, Cross-sectional cut 3 at the base of proximal aneurysm. The multiple holes encircling the specimen represent the location of the stent wires, which have been removed. The thin layer of tissue deep to these holes and forming the inner surface of the carotid is neointimal proliferation formed in response to the stent wires. At the *top* is the cut fibrous base of the proximal aneurysm.

with proximal parent artery occlusion (11). Extracranial-to-intracranial bypasses were performed in 25 of the patients to provide adequate distal cerebral perfusion. They achieved complete thrombosis of the aneurysms in 78% of their cases with 1.5% morbidity and concluded that proximal balloon occlusion of the parent vessel is both safe and effective for surgically unclippable aneurysms.

In 1992, Graves et al described the flow dynamics of lateral carotid artery aneurysms created in dogs and their effects on coils and balloons (5). Forty aneurysms were created in 14 dogs. Hemodynamic flow effects within these aneurysms were evaluated with angiography and color Doppler, both before and after placement of coils and balloons. They observed three distinct zones of flow associated with these aneurysms: (*a*) an inflow zone entering at the distal wall of the aneurysm ostium; (*b*) an outflow zone exiting at the proximal ostium; and (*c*), a central, slow-flow vortex. These flow effects were also observed in our model of lateral carotid aneurysms before stent placement. Graves described three techniques that modified the inflow zone to thrombose the aneurysm while preserving the parent artery: (*a*) complete filling (packing) of the aneurysm with coils or balloons; (*b*) obstruction of the inflow by coils or balloons; and (*c*) displacement of the inflow. The force of blood at the inflow zone was considerable; in four aneurysms this force resulted in displacement of the coils from the lumen of the aneurysm into the parent artery. The effect of flow within the aneurysm on the balloon was also significant and sometimes resulted in shifting its position; however, if the balloon packed the aneurysm lumen completely and no inflow zone was present, complete occlusion of the aneurysm occurred without balloon shifting.

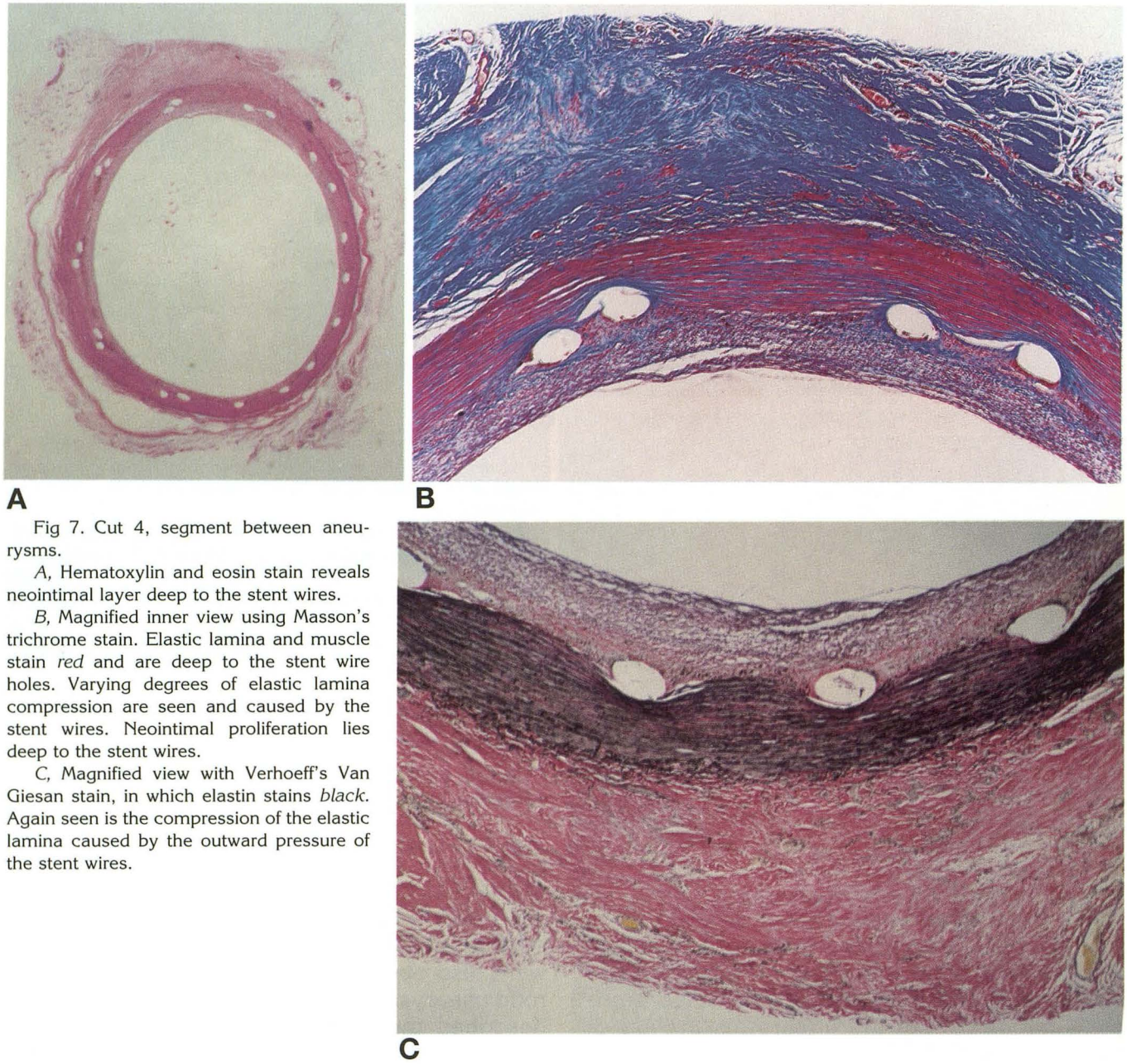

Fig 7. Cut 4, segment between aneurysms.

A, Hematoxylin and eosin stain reveals neointimal layer deep to the stent wires.

B, Magnified inner view using Masson's trichrome stain. Elastic lamina and muscle stain *red* and are deep to the stent wire holes. Varying degrees of elastic lamina compression are seen and caused by the stent wires. Neointimal proliferation lies deep to the stent wires.

C, Magnified view with Verhoeff's Van Giesan stain, in which elastin stains *black.* Again seen is the compression of the elastic lamina caused by the outward pressure of the stent wires.

Displacement of the inflow zone occurred when a balloon or coils were placed in a proximal aneurysm of a tandem set of two aneurysms. This displacement of the inflow zone was observed in the distal of the two aneurysms and markedly decreased the distal aneurysm because of indwelling thrombus formation. Aneurysms that did not demonstrate displacement of the inflow zone did not show any decreases in size. They concluded that modification of the inflow zone by blocking or displacing it can produce thrombosis of an aneurysm with preservation of the parent artery.

Porous metallic stents placed across the aneurysm necks (as in our experiment) change the usual mechanical flow characteristics within the aneurysm lumen (Fig 9). Usual inflow and outflow effects were not seen on angiography after stent placement; instead, gradual puddling of blood and contrast medium was observed immediately after deposition of the stent. This trapping of blood within the aneurysm led to fibrotic growth and organization and eventual ablation of the aneurysm pouch, as documented in our histopathologic studies. In addition, the stent did not cause occlusion of the

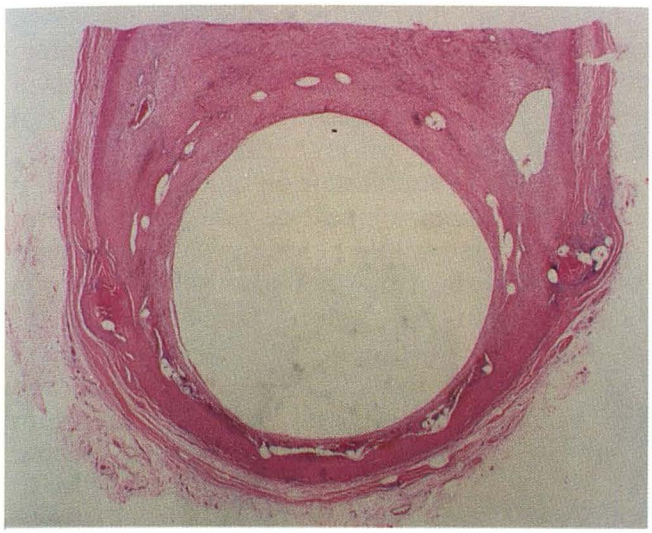

Fig 8. Cut 6 through the midbase of the more distal aneurysm. Hematoxylin and eosin stain reveals mature fibrous connective tissue at aneurysm base (*top*), neointimal proliferation deep to the stent wire holes, and vessel lumen patency.

carotid artery; thus, occlusion of the aneurysm pouch was achieved without entering its lumen and diminished the possibility of aneurysm rupture. A thin layer of neointima surrounded the stent wires, but no definite organized clot within the carotid lumen was documented. Verdon et al reported their findings with electron microscopy in 18 iliac arteries in canines after percutaneous placement of an endovascular stent (Verdon SL, Gould PE, Termin PL, et al, Scanning Electron Microscopy of a Self-Expanding Vascular Stent in a Canine Animal Model, presented at the XIIth International Congress for Electron Microscopy, San Francisco, Calif, 1990). At 21 and 28 days after stent placement there was an increase in endothelial cell coverage over the stent wires, which were bridged with endothelial cells. The resulting intraluminal surface of the iliac artery after 28 days appeared much like a complete endothelial surface (neointima). Other studies have shown similar findings of reendothelialization in canine models (12) (Palmaz JC, presented at the joint meeting of the Cardiovascular and Interventional Radiological Society of Europe and the Society of Cardiovascular and Interventional Radiology [USA], Sardinia, Italy, May 1987). The intimal hyperplasia seen in our study and noted by others warrants further physiologic investigation into how the arterial wall reacts to stent placement.

Patency rates for vessels treated with intravascular stents depend greatly on the intraluminal diameter of the vessel. Immediate or delayed occlusion is more likely in smaller caliber vessels (eg, coronary or infrapopliteal arteries) (13–16). Early vessel occlusion is caused by platelet aggregation and subsequent thrombosis incited by the stent wires. Palmaz et al revealed that the amount of fibrin-platelet thrombus deposition is proportional to the total metal surface of the stent (17). Thus, the amount of thrombus is relatively constant for a given stent under different degrees of expansion. Stents expanded to larger diameters would spread the thrombus over a proportionately larger surface than in smaller-diameter vessels. Therefore, thrombus aggregation in a small-caliber vessel possibly could reduce blood flow to a degree conducive to further propagation of clot and subsequent vessel occlusion.

Puel et al and Sigwart et al recently reported thrombosis rates of 39% and 11%, respectively, after coronary stent placement (17–19) Serruys et al experienced 24% complete occlusions of stented coronary arteries (15). In contrast, there was a less than 2% incidence of thrombotic occlusion in 171 stents placed into diseased iliac arteries from a multicenter clinical trial (20, 21).

The stented carotid arteries in our animals remained widely patent, with no incident of occlusion, despite their relatively small intraluminal diameters (3 to 4 mm). Our patency rates did not reflect those noted in clinical trials regarding stent placement in human vessels of similar caliber. Possible explanations for this discrepancy include the lack of atherosclerotic disease in the vessels of the animals in this experiment versus severe disease in the stented human arteries, and the small number of vessels stented in this study.

The ability to ablate an aneurysm by an endovascular approach and without entering its lumen is an attractive possibility. The potential risk of rupturing the aneurysm while packing its lumen with coils or balloons would be avoided. Furthermore, coils or balloons may protrude into the native vessel, which could compromise its intraluminal diameter or act as a nidus for thrombus formation. On the other hand, stent wires line the inner surface of the vessel wall, thus causing minimal if any narrowing of the vessel lumen.

Success with stents depends on placement of the devices across the mouths of aneurysms.

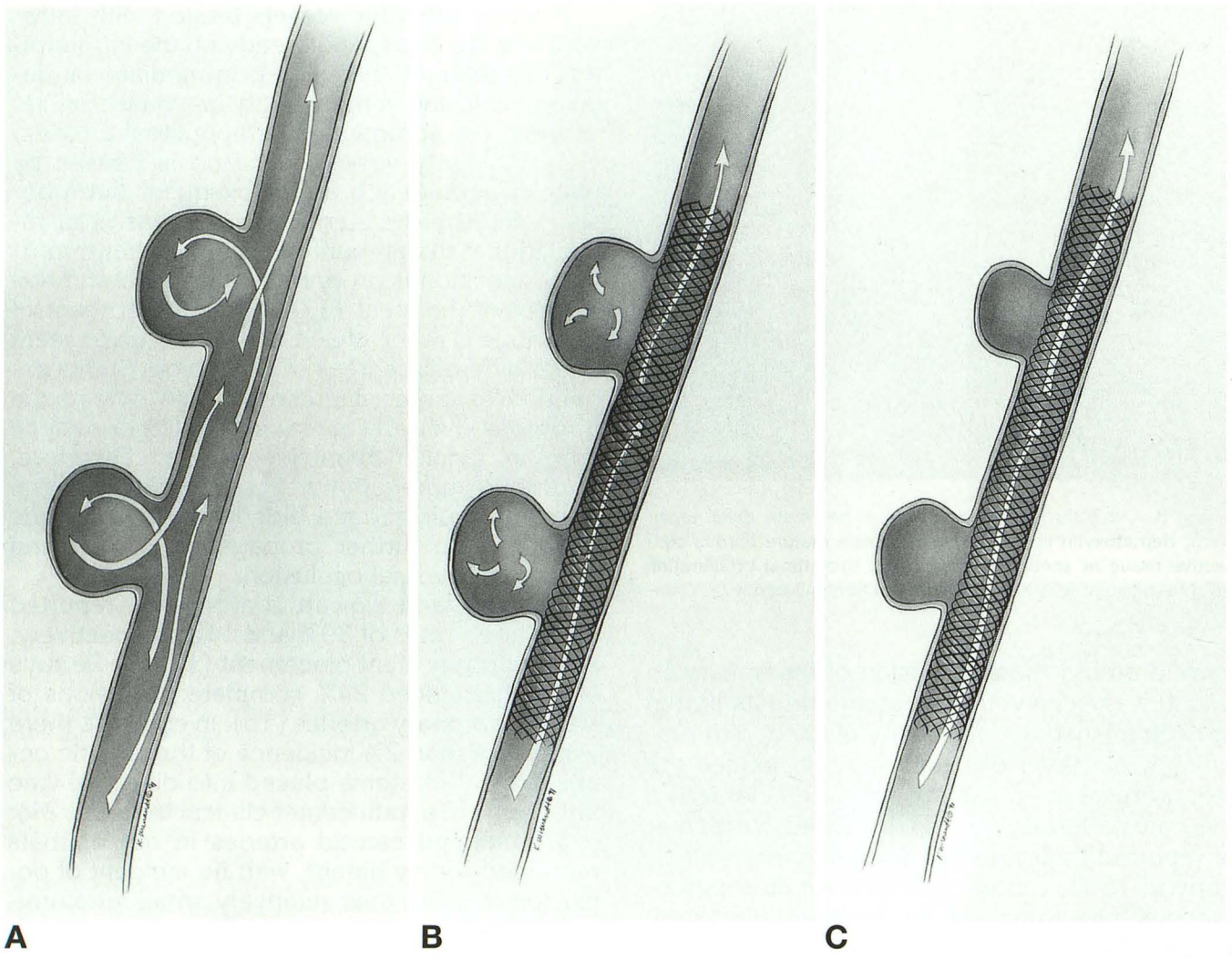

Fig 9. Flow effects before and after stent placement.

A, Carotid/aneurysm model with *arrows* demonstrating blood flow patterns. Vortex flow pattern is present within the aneurysm lumen, whereby inflow is along the distal aneurysm wall and outflow along the proximal wall.

B, Immediately after stent placement, vortex flow pattern within the aneurysm is disrupted. There is stasis and subsequent pooling of blood within the aneurysm lumen. The stent does not affect carotid artery patency.

C, Delayed arteriogram (8 weeks after stent placement) reveals absence of filling of the previously demonstrated aneurysms. This is caused by thrombus formation and organization. The carotid artery remains patent.

This may not be possible with aneurysms that lie at the bifurcation point of a vessel, a common location for aneurysms in the intracranial circulation. Thus, current stent systems may be inadequate for treatment of these aneurysms, which could be better treated with endovascular packing. Possibly, stents could be used in treatment of large lateral aneurysms near the skull base or in the distal carotid or vertebral arteries. The stent system used in our experiment was mounted on a 7-F introducer catheter, which would be too large for intracranial applications. A smaller version, possibly reduced to 4 F, might have the flexibility and size to treat skull base aneurysms adequately. Development of the ideal stent system for intracranial applications was beyond the scope of this experiment, in which the purpose was to determine the feasibility of treating lateral aneurysms with stents while preserving vessel patency.

Conclusion

There are many advantages to treating aneurysms via an endovascular approach. A transvascular approach obviates the need for a major

invasive surgical procedure with the risks associated with general anesthesia, making it a less-invasive procedure, and entailing less discomfort and a shorter recuperation time for the patient. Medical costs for treating aneurysms in this fashion would be significantly reduced. Current endovascular approaches used in the treatment of aneurysm entail either packing the aneurysm (eg, with balloons or with metal coils), or completely occluding the native vessel. Packing the aneurysm can be potentially dangerous; the aneurysm wall is often fragile and may rupture. Occluding the parent vessel that harbors an aneurysm may cause immediate or delayed ischemic complications.

Altering the usual flow patterns within aneurysm lumens may lead to stasis of blood, thrombus formation, and subsequent organization and fibrous formation eventually causing ablation of the aneurysm. In our model, stents were used to alter blood flow within the aneurysm lumen by providing a mechanical hinderance to the usual vortex flow pattern while maintaining patency of the native vessel. Histopathologic study revealed mature fibrous connective tissue and collagen, indicating a well-organized thrombus filling each aneurysm lumen.

Possibly, stents will be included in the armamentarium of endovascular devices currently used in the treatment of selected intracranial aneurysms.

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