

## HISTORICAL VIGNETTES IN VENOUS SURGERY

Norman M. Rich, MD, Section Editor

## Polytetrafluoroethylene large vein replacements and high-altitude treks: Footnotes and footprints from Ben Eiseman's panoply of interests

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The late Ben Eiseman (November 2, 1917–November 19, 2012), Emeritus Professor of Surgery and Medicine at The University of Colorado, will be remembered for his passionate devotion to both surgical science and mountaineering. His passion took him to many high places, including the summits of all 54 of Colorado's "fourteeners," the Matterhorn (14,690 ft [4478 m]) and Mt Kilimanjaro (19,340 ft [5895 m]; Fig 1). He also climbed to the 17,000+ ft (5182+ m) base camps on the east side of Mt Everest and Pakistan's K2, the world's second-highest mountain. The same zeal and innovative approach applied to teaching and research led to world-wide recognition and his performing surgical operations in at least 12 different countries. Ben viewed daunting flat rock faces and surgical dilemmas as equal opportunities to develop new paths for others to follow. He approached each situation with careful study and scientific reasoning, eschewing daredevil adventurism, although the last was not always apparent to casual observers.

## HOPEFULLY, GORE PICKED UP THE TAB

The Gores and Eisemans often skied together, and Wilbert L. Gore chose a 1970 après ski Aspen dinner to demonstrate to Ben and Mary Eiseman the inert nature and limited permeability of expanded polytetrafluoroethylene (PTFE), then used primarily as a dielectric covering and now trademarked as GORE-TEX.<sup>1</sup> The setting and presence of their wives were propitious, as Gore was

seeking advice regarding both its potential as an artery substitute and as a stain-resistant garment. Eiseman took various forms of the material back to the laboratory and studied its biologic inertness and negative surface charge, finding it to be minimally cytotoxic and more negatively charged than Dacron.<sup>2</sup> He and his colleagues then worked in tandem with the Gore Company and other authors to optimize its thickness and porosity as a vascular substitute, implanting grafts ranging from 2.8 to 6 mm in the carotid and femoral arteries of dogs and 6 to 9 mm in the larger veins of pigs. Gore eventually selected pore sizes of 20 to 30  $\mu$ m (Fig 2) as being optimal for sustaining a thin pseudointima and prolonged patency.<sup>3</sup> Larger pore sizes were associated with capillary and fibrous tissue build-up within the lumen and ultimately poorer patency.

Their early arterial results should have been discouraging because the grafts routinely induced intimal hyperplasia at the anastomotic margins, resulting in occlusion within 4 to 6 weeks, but Eiseman simply set this unforeseen problem aside. He had been eager to try PTFE in the more thrombus-prone venous system, and here was the opportunity. He and Singaporean Professor K. S. Yeoh had performed the first prosthetic interposition portal caval "H-graft" in 1960 during one of Ben Eiseman's many extended sabbaticals.<sup>4</sup> The patient had a splenectomy for hypersplenism 2 years previously and was now having recurrent variceal bleeding. When the portal vein was opened, it was found to be completely thrombosed at the liver hilum with patent and engorged superior mesenteric veins. The thrombotic plug was easily removed, but the inferior vena cava (IVC) and portal vein could not be brought into apposition, so a three-quarter-inch length of one-half-inch woven Teflon tubing was used to bridge the gap. The patient had no further hematemesis for about a year and then rebled, suggesting that the shunt had then occluded.

Eiseman's laboratory had a substantial experience with swine, as it was winding down a series of studies conducted over 7 years in which isolated porcine livers, spleens, and ventilated lungs maintained their normal functions when perfused with normothermic human blood, suggesting they could serve as extracorporeal temporary substitutes

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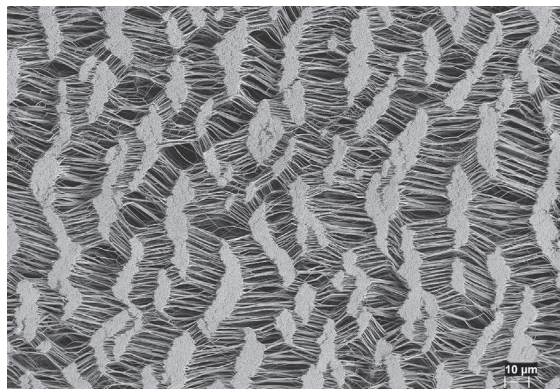


**Fig 1.** Mary and Ben Eiseman, preparing to climb to Mount Kilimanjaro's Kibo summit, on Tanzania's northern border with Kenya in 1973.

for patients with potentially reversible organ failure.<sup>2,5</sup> There were sufficient short-term partial successes with livers in moribund patients to encourage continuation, but in the end, the failed human organs needed replacement rather than *ex vivo* surrogate bridging with an expectation of functional recovery.

#### PTFE IN LARGER PORCINE VEINS AND CAUTIOUS TRANSITIONING TO PATIENTS

The portal veins of 14 pigs were excised and replaced with 6- to 9-mm-diameter PTFE tubes to be compared with similar-sized woven Teflon grafts in four additional subjects.<sup>6</sup> Pigs are less coagulation prone than dogs, but three of the four woven Teflon portal vein grafts thrombosed within 2 weeks, whereas 13 of the 14 PTFE portal grafts were patent for varying periods out to 6 months. Another 13 pigs were used to implant PTFE tubes as replacements for excised segments of external iliac veins



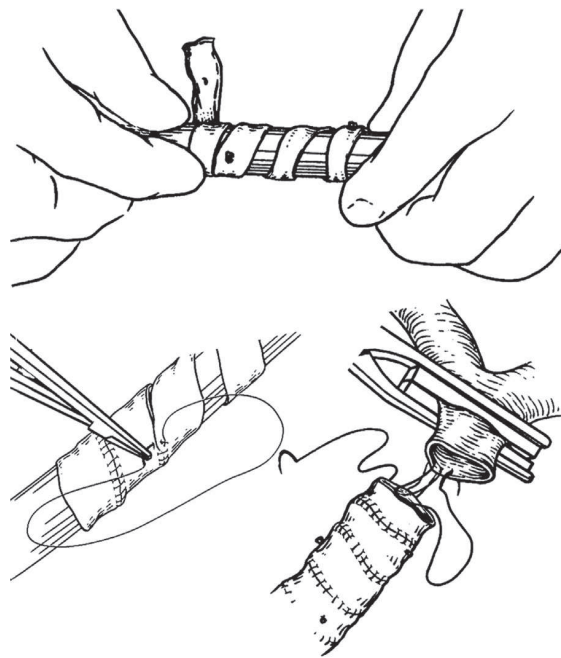
**Fig 2.** Scanning electron micrograph of 20- to 30-μm pore GORE-TEX (original magnification, 500×).

and excisions at varying IVC levels extending from the common iliac confluence to just below the right atrium. Only two grafts occluded within 2 to 6 months; both were in the infrarenal IVC. Others would find that PTFE substitutes for both the SVC and IVC remained patent without anticoagulation for 7 to 9 months in dogs but thrombosed within 1 to 2 days when implanted as canine femoral vein substitutes.<sup>7</sup>

Eiseman's results, however, were sufficiently encouraging to consider using 9-mm PTFE tubes clinically to replace portal veins that were partially encircled but not invaded by cancer for en bloc excision along with the pancreas and duodenum. Over the next 2 years, three patients were identified with pancreatic cancers that appeared to be appropriate for this extended procedure. One patient died 3 years later of coronary thrombosis with a patent graft, and another had an unobstructed graft imaged at 17 months and was later known to have survived for at least 32 months. A third patient was retrospectively inoperable and died on the 10th postoperative day, albeit with an open graft.<sup>6,8</sup>

#### AN AUTOGENOUS ALTERNATIVE

In 1974, Chiu et al,<sup>9</sup> at McGill University, introduced spiral saphenous vein grafts for SVC replacements in dogs, providing a diameter-matched endothelialized surface. The graft preparation (Fig 3) was tedious and time consuming, but multiple SVC grafts remained patent for 10 to 13 months. A quarter of a century later, Doty, Flores, and



**Fig 3.** Construction of a larger-diameter spiral vein graft from a longitudinally slit saphenous vein, in this instance, for superior vena cava replacement (adapted from Doty et al<sup>10</sup>).

Doty<sup>10</sup> reported on 16 patients with nonmalignant SVC obstructions bypassed with spiral saphenous vein grafts and no coagulation suppression other than aspirin. Fibrotic mediastinitis accounted for 11 cases, of which seven had caseous necrosis; four were central venous catheter-related, and one was a spontaneous thrombosis. Patency out to 23 years was observed in 14 grafts. Aggressive mediastinal fibrosis compressed one graft during the first post-operative year, which then required three subsequent graft revisions over 12 years. Another patient was asymptomatic for more than 11 years until the graft was destroyed during a coronary artery bypass. It was replaced with a straight saphenous vein graft that produced transient SVC syndrome recurrence.

#### EXTERNAL RING-SUPPORTED PTFE

Although PTFE grafts typically acquire a pseudointima, it is not as thrombo-protective as the real thing, and there is often insufficient pressure in the venous circulation to prevent graft collapse with potential to form wall-to-wall synechiae. Gore responded to this concern by adding an external supporting spiral of semirigid rings. These grafts were tested in dogs as iliac vein replacements with and without temporary upstream arteriovenous fistulas.<sup>11</sup> Grafts without a fistula occluded within a week. Those with fistulas had the fistula ligated after 2 weeks, and 9 of 12 remained patent for at least 4 months. The authors used a similar strategy plus warfarin to protect a clinical external ring-supported PTFE common iliac vein bypass, ligating the fistula after 3 months with no loss of patency. They concluded that the arteriovenous fistula was a key component, which was true — but perhaps just for dogs. Quinones-Baldrich et al's<sup>12</sup> recent report of 47 IVC reconstructions after en bloc retroperitoneal tumor resections included 18 patients with extensive external ringed PTFE IVC and renal vein replacements, which had a 5-year cumulative patency of 80% with no fistulas and only aspirin for anticoagulation. Although spiral vein grafting still has a role in infected fields, externally supported PTFE has allegorically summited, offering expediency, superior compression resistance, and similar long-term patency.

#### BIOLOGY IS KING, SELECTION IS QUEEN: TECHNICAL MANEUVERS ARE [JUST] THE PRINCE AND PRINCESS<sup>13</sup>

Eiseman's extended pancreaticoduodenectomy has no dearth of naysayers but is still in use and often extended to include superior mesenteric veins. Emory University and the Minnesota and Florida Mayo Clinics identified 33 such patients operated on between 1994 and 2009, 28 of whom had T<sub>3</sub> or higher pancreatic adenocarcinomas.<sup>14</sup> PTFE replacement of the portal and superior mesenteric vein was required in 49%, with graft diameters ranging from 8 to 20 mm, 73% of which were externally supported. The 30-day mortality was 6%, and the morbidity rate was 46%, with pancreatic fistulas occurring in just 9%. Graft patency was 76% at 14 months, but the

median survival for pancreatic adenocarcinoma patients was just 12 months. This procedure will be stuck at the base camp until new knowledge about pancreatic cancer's biology leads to effective collateral therapy.

PTFE interposition H-graft portal systemic shunts are about three-quarters of the way up the mountain, and PTFE-covered stent transjugular portal systemic shunts (TIPS) are straggling behind. Rosenmurgy et al's<sup>15</sup> 18-year follow up of 132 cirrhotic patients with similar distributions of Child class and Model for End-stage Liver Disease (MELD) scores randomized to have 8-mm external ring-supported PTFE H-graft shunts or bare metal stent TIPS dilated to 8 to 10 mm showed a significant survival advantage for H-grafting but only for Childs Class A (91 vs 19 months) and B patients (63 vs 21 months). Shunt failure, defined as irretrievable occlusion, recurring variceal hemorrhage, or liver failure requiring transplantation was associated with 91% mortality. It occurred significantly later after H-grafting (45 vs 19 months for TIPS). Doppler ultrasound surveillance has subsequently shown that PTFE-covered TIPS stents have better flow characteristics than bare stents and hence may have the potential to narrow this temporal gap, but, at a minimum follow-up of 13.4 years, 88% of the patients in both of Rosemurgy's groups had already died.

#### LEARNING FROM THOSE WHO FAIL TO SUMMIT?

Mountaineering is in many ways a valid metaphor for Dr Eiseman's approach to surgical research. The breadth of his research interests was spectacular, unlikely ever to be equaled, and overlapped his mountaineering experience as head of the Safety Committee of the Colorado Outward Bound School and when he became involved in evacuating two fellow climbers on Muztagh Ata (24,636 ft [7509 m]), on the northern edge of the Tibetan Plateau. One had been struck by lightning and the other had developed cerebral edema at an altitude of about 19,000 ft.

A mountaineer's goal is to reach the summit, whether the mountain is Everest or a benign hill rising from the plains. The more difficult the ascent, the greater the need for preparation and training, and the greater the risks, the greater the determination to reach the summit. Poor judgment, the wrong equipment, or bad weather may result in a temporary setback or an irretrievable disaster. Surgical research commonly suffers setbacks, but they usually pose new questions, are rarely disasters, and are valued as important steps toward discovering new knowledge.

Since 1951, the American Alpine Club (AAC) of Golden Colorado has been publishing annual reports, cumulatively updating all the mountaineering accidents in North America. Each accident — like a case presentation in a surgical Mortality & Morbidity conference — is analyzed according to the conditions before the accident, the cause of the accident, and the judgment before, during, and after its occurrence. As a member of the AAC, Ben Eiseman received *Accidents in North American Mountaineering* every year. These reports and “Eiseman M & Ms”

were built on the same principles: probe relentlessly for the truth, identify and learn from the errors.

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