Surface-modified coils and new filling materials seem to reduce the recanalization rate in these difficult-to-treat aneurysms, while reconstruction of the parent artery in conjunction with the use of stents can successfully treat many complex and wide-neck aneurysms.

New tools and techniques, such as horizontal stenting of bifurcation aneurysms, reconstruction of dysplastic arteries, virtual stenting, and dense packing of the vessel with coils, are improving endovascular outcomes. A new neurovascular microstent, the Cordis Enterprise stent, composed of nitinol, with a closed cell design, was specifically developed for the treatment of wide-necked intracranial cerebral aneurysms. Flow diverters coupled with digital subtraction angiography (DSA) are being used in order to divert embolic material away from the arteries that carry blood to the brain.

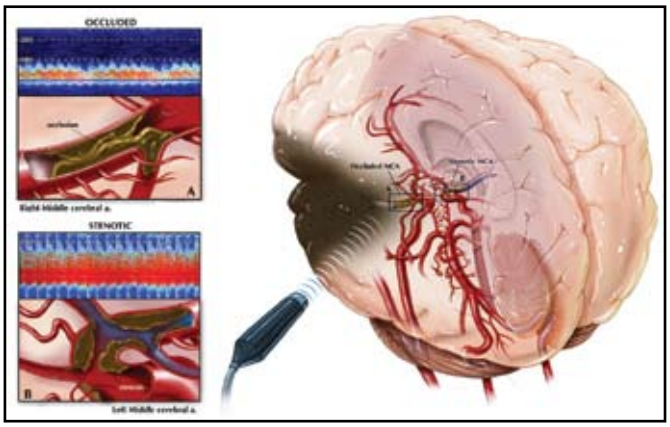
Endovascular techniques will continue to grow in their application to the treatment of intracranial aneurysms. In the future, hybrid imaging technology and robotic enhancement of angiographic instruments will add precision and improve reproducibility. Continuous improvements in coil design—eg, enhanced coils—are making endovascular treatment safer and decreasing the recanalization rate. Parent artery reconstruction will become a major component of endovascular treatment, while new flow diverters will produce a paradigm shift from endosaccular obliteration of the aneurysm to endoluminal repair of the parent artery.

Stroke in Sickle Cell Disease: Recent Successes

The reported incidence of all types of stroke in childhood is relatively low, with 2.6 occurring per 100,000 white children and 3.1 per 100,000 in black children (Broderick et al. *Child Neurol* 1993). However, additional analyses indicate that children with sickle cell disease (SCD) face a huge relative risk of ischemic stroke compared with a healthy population (RR=220; Earley et al. *Neurology* 1998). Chronic blood transfusion therapy has been employed as secondary prevention of stroke in patients with SCD for over 30 years. This session discussed the epidemiology of SCD as well as the risks and benefits of using chronic transfusion therapy in primary stroke prevention.

Robert J. Adams, MD, Medical University of South Carolina, Charleston, SC, gave an overview of the Stroke Prevention Trial in Sickle Cell Anemia (STOP). Transfusion of every child with SCD is not warranted due to the high number needed (200) to save one child from a stroke, side effects, inconvenience to families, and cost. The STOP trial therefore sought to identify children at highest risk of stroke using transcranial Doppler ultrasound (TCD; Figure 1). Children were screened using TCD, and those with 2 measurements ≥200 cm/s were randomized to either periodic transfusion or standard care (including occasional transfusion). The study found that periodic transfusion reduced the risk of stroke by 92%, reduced other complications, and led to better height and weight gain (Adams et al. *NEJM* 1998).

Figure 1. Stroke Risk Identification Using TCD.



The presentation by Heather Fullerton, MD, University of California, San Francisco, CA, addressed whether the STOP trial findings influenced treatment of SCD patients. Using a California-wide database, Dr. Fullerton and colleagues found a downward trend in strokes in patients with SCD post-1998, the year that the STOP results were published. Data from a Kaiser Permanente cohort showed an upward trend in the numbers of SCD patients obtaining a first TCD post-1998, suggesting that the decrease in strokes were related to the identification of high-risk patients. "We definitely have some cause for optimism. We think that the stroke rates are declining, and we think this is due to implementation of this primary stroke prevention strategy," commented Dr. Fullerton. Obstacles remain, however. In a survey of 207 hematologists, 9 of 10 reported issues with acquiring TCDs, citing poor patient adherence and lack of facility availability. "This is really an issue for our neurology community, who is trying to make this [technology] increasingly available to these children," said Dr. Fullerton.

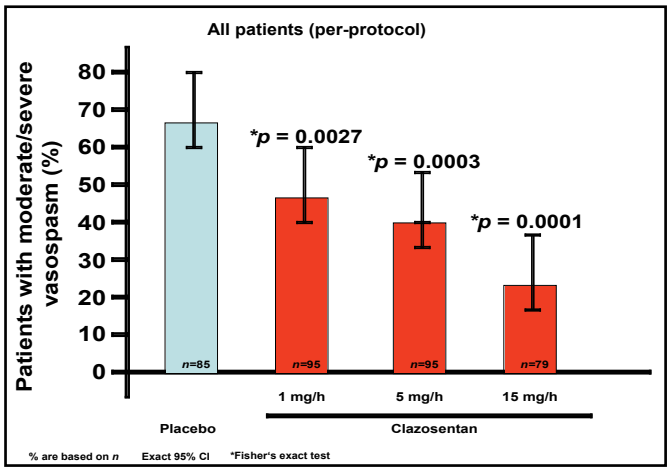
Michael DeBaun, MD, MPH, Washington University, St. Louis, MO, gave an overview of silent cerebral infarctions and future research in SCD-associated stroke prevention. Silent cerebral infarct is defined as an increased signal on T2-weighted imaging that is not accompanied by focal neurologic deficits. "We think about one-fifth of children

who have a diagnosis of hemoglobin SS will have a silent cerebral infarct before their 18th birthday," said Dr. DeBaun. Silent strokes cause significant cognitive deficits in these patients, leading to problems in learning and poor school performance. The objective of the Silent Cerebral Infarct Transfusion Trial (SITT) is to determine if prophylactic transfusions will result in a reduction of both clinically evident and silent strokes in children with SCD. The trial is ongoing, has randomized 127 patients to date, and will last approximately 6 years. The results of this trial should provide valuable insight into the natural history of SCD and further the understanding of the risks and benefits of transfusion therapy.

Vasospasm and Neuroprotection

Subarachnoid hemorrhages that result from ruptured aneurysms initiate a series of events that may result in very poor outcomes. R. Loch MacDonald, MD, University of Toronto, Toronto, Ontario, Canada, gave an overview of the biological mechanisms of vasospasms that result from ruptured aneurysm blood clots. "The erythrocyte seems to be the component of the blood that is primarily responsible for initiating the delayed angiographic response that occurs," said Dr. MacDonald. The vasospasms are related to smooth muscle contraction, possibly due to increases in endothelin or prostaglandins, decreases in the relaxant nitric oxide, neurotransmitters, membrane depolarization, increased sensitivity to calcium, or impairment of muscle relaxation pathways. Barth et al (*Stroke* 2007) conducted a study of the calcium channel blocker nicardipine in 32 patients undergoing craniotomy for aneurysm. Nicardipine pellets (40 mg) were placed in the basal cisterns of 16 patients. On Day 8, the incidence of vasospasms in the nicardipine-treated patients was reduced from 73% to 7% ($p<0.05$) and mortality between treated (6%) and placebo patients (38%) reached statistical significance ($p=0.042$). "This fits with the depolarization mechanism of vasospasm," noted Dr. MacDonald. In preclinical models, endothelin antagonists are successful in preventing vasospasm. This was confirmed in the phase 2 CONSCIOUS-1 study. Three doses of clazosentan were used to treat patients with subarachnoid hemorrhage, and all 3 doses were significantly better than placebo in preventing vasospasm (Figure 1). In addition to the effects of the blood clot, secondary processes such as disturbance of the blood brain barrier, hypertension, brain edema, apoptosis, and global ischemia are at play. "It starts to become even more complicated when you add in these other mechanisms…all can contribute to ischemia, infarction, and poor outcome," said Dr. MacDonald.

Figure 1. Clazosentan Prevents Cerebral Vasospasm.



Given the serious consequences of vasospasm, researchers have proposed performing angioplasty as prophylactic treatment. Richard Latchaw, MD, University of California, Davis, CA, presented work from Jonathan Hartman, MD, Kaiser Permanente Sacramento Medical Center, Sacramento, CA, that explored this approach. "This is a dangerous procedure…every time I do angioplasty on a post-subarachnoid hemorrhage patient, I really respect those vessels because they are very tender vessels. It's very easy to produce overdilitation and rupture," cautioned Dr. Latchaw. The Balloon Prophylaxis of Aneurysmal Vasospasm (BPAV) study was a phase 2 trial that was conducted to determine if prophylactic angioplasty performed within 96 hours of a Fisher grade III or III+IV subarachnoid hemorrhage would alleviate vasospasm. The study enrolled 170 patients and was conducted at 10 centers in the US, Canada, and the Netherlands. Based on 3 deaths that occurred during the study, the protocol was modified to exclude A1 and P1 segments, as it was believed that these were too dangerous. A total of 81 patients received prophylactic angioplasty, with 1 perforation and 3 deaths. There was no statistically significant difference between the group that received balloon angioplasty and the control group in terms of vasospasm, outcomes at 3 months, length of hospital stay, or the probability of delayed ischemic neurological deficits. "One of the confounding factors is that the ballooned patients tended to have a higher degree of hydrocephalus, which may have made that group look a little worse," noted Dr. Latchaw. However, the need for therapeutic balloon angioplasty was significantly higher in the control group ($p=0.03$). "This is the most significant part of this study," concluded Dr. Latchaw.