

Current Issues in Vascular Disease

*Highlights from the 11th Annual Meeting of the Society for Vascular Medicine and Biology
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The 11th Annual Meeting of the Society for Vascular Medicine and Biology featured symposia on contemporary issues in vascular disease. Important topics discussed included aneurysmal disease, gene therapy for arterial insufficiency, mesenteric vascular disease, and lymphedema.

Aortic Aneurysms

M. David Tilson, MD, from Columbia University College of Physicians and Surgeons, focused on the molecular biology of aortic and arterial aneurysms, reporting that studies from his laboratory suggest that immunoglobulins directed against major proteins in the vessel wall may contribute to the pathogenesis of aortic aneurysms. There may be an autoimmune basis for aortic aneurysms in patients with a familial history of this disorder. In particular,

affected individuals commonly share the DR-2 allele for the major histocompatibility complex class II gene.

Jack L. Cronenwett, MD, from Dartmouth-Hitchcock Medical Center, in discussing the natural history of aortic aneurysms, noted that annual enlargement of aortic aneurysms approximates 10% of the diameter. The annual rupture rate depends on the size of the aneurysm. Contributing factors for aneurysm rupture include the rate of expansion of the aneurysm, hypertension, smoking, and a history of abdominal aortic aneurysms affecting a first-degree relative. Pending a decision to operate, medical therapy should include β -adrenergic blockers. Dr. Cronenwett recommended ultrasonographic surveillance of aneurysms approximately every 3 to 6 months to assess the rate of expansion.

Michael L. Marin, MD, from Mount Sinai School of Medicine, reviewed the status of endoluminal stent-graft repair as an alternative to aneurys-

mectomy. Currently, about 5% of infrarenal abdominal aortic aneurysms are suitable for this endovascular approach, which entails placement of a tube or bifurcated graft made of Dacron or polytetrafluoroethylene with a stent framework of nitinol or stainless steel. Outcomes following use of these devices are being assessed in clinical trials, and long-term success rates are not yet available. Potential complications include leaks into the aneurysm sac, embolization, or a material disruption of the graft.

Gene Therapy for Arterial Insufficiency

Gene therapy for peripheral arterial disease has received considerable attention in both the scientific literature and lay press. The molecular biology of angiogenesis, discussed by Kenneth Walsh, MD, of Tufts University School of Medicine, included a review of much of the basic information underlying the development of gene therapy pro-

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grams. Dr. Walsh defined *angiogenesis* as the formation of new capillary vessels and *arteriogenesis* as the development of collateral vessels, noting that circulating endothelial progenitor cells contribute to the growth of new blood vessels in the adult. Angiogenesis is mediated by a variety of growth factors, including vascular endothelial growth factor (VEGF) and fibroblast growth factor. VEGF, for example, stimulates the protein kinase Akt that promotes cell survival and also activates nitric oxide synthase to produce nitric oxide.

Steven E. Epstein, MD, from Washington Hospital Center in Washington, DC, reviewed the clinical trials that have examined the efficacy of gene therapy. Of 8 published clinical trials, only 2 have been large and randomized, and these included patients who had symptomatic coronary artery disease. Although neither trial demonstrated the superiority of angiogenic factors over placebo, these are early studies, and the results, should not create pessimism. It may be necessary for a combination of growth factors to be administered to promote angiogenesis. Concerns raised about angiogenic therapy include its potential to affect blood vessels adversely, such as contributing to the formation of neointimal thickening. In addition, there is the potential for these drugs to promote tumor growth.

The ethical and regulatory aspects of gene therapy were discussed by Lucio Luzzatto, MD, of Memorial Sloan-Kettering Cancer Center. Among the important points raised by Dr. Luzzatto were the need to fastidiously follow standards of good clinical research, to make realistic predictions and claims, and to avoid conflicts of interest.

Mesenteric Vascular Disease

An often ignored—yet important—vascular problem is that of mesenteric

vascular disease. In a symposium on this topic, Bruce Gray, DO, of the Cleveland Clinic Foundation, and John R. Laird, MD, of Washington Hospital Center, reviewed the clinical assessment and management of mesenteric ischemia.

Acute mesenteric ischemia—which often occurs as a consequence of an arterial embolism and, as such, may complicate atrial fibrillation, cardiomyopathy, or myocardial infarction—is typically a surgical emergency, often requiring resection of the affected portion of bowel. Chronic mesenteric ischemia is usually caused by high-grade stenoses or occlusion of the 3 principal mesenteric arteries, including the celiac, superior mesenteric, and inferior mesenteric arteries. Diagnostic studies to assist in the evaluation of chronic mesenteric ischemia include CT, MRI, visceral duplex ultrasonography, endoscopy, and angiography.

Dr. Gray noted that mesenteric venous thrombosis accounts for 5% to 25% of the cases of intestinal ischemia and is associated with a mortality rate that ranges from 15% to 80%. Thrombus in the mesenteric vein may be related to inflammation or infection, elevated mesenteric venous pressure, or complications of a hypercoagulable state. Management of mesenteric ischemia includes volume resuscitation, anticoagulation, and surgical resection of the affected portion of bowel.

Lymphedema

A symposium on lymphedema reviewed current concepts in the diagnosis and treatment of this disorder. Thomas Rooke, MD, from the Mayo Clinic, noted that lymphedema typically occurs as a consequence of lymphatic obstruction. In addition to the primary (idiopathic) form of lymphedema, secondary causes include cancer, trauma, infection, and parasites. Clinical stages of lymphedema include an early pitting stage and a late fibrotic, nonpitting stage, often complicated by verrucous lesions. Treatment is required to improve function, decrease pain, prevent infection, and improve appearance. Leg elevation, pumps, massage, or a combination of these are among the therapies to limit the amount of lymphedema. Elastic support stockings and other compressive devices can be used to prevent exacerbation of this condition.

Peter Gloviczki, MD, also from the Mayo Clinic, discussed several diagnostic tests to assist in the evaluation of lymphedema. Two of these are lymphoscintigraphy and lymphangiography. He noted that surgical therapies are used occasionally but, at the current time, are not appropriate for most patients. These treatments include lymphatic-lymphatic bypass and lymphovenous bypass as well as debulking procedures. ■

Main Points

- There may be an autoimmune basis for aortic aneurysm formation in patients who have a familial history of this disorder.
- Angiogenesis is mediated by a variety of growth factors, including vascular endothelial growth factor and fibroblast growth factor.
- Acute mesenteric ischemia often occurs as a consequence of an arterial embolism; as such, it may complicate atrial fibrillation, cardiomyopathy, or myocardial infarction.
- Early studies with gene therapy for arterial insufficiency have been disappointing.