ETIOPATHOGENESIS AND IMMUNOLOGIC FACTORS

CFIDS is a highly heterogeneous condition which is unlikely to be explained by a single etiologic agent. Although viral sequences have been detected in the lymphocytes of CFIDS patients, it is unclear whether they are cause, effect, or epiphenomena. While Epstein-Barr virus, *Candida* sp, *Brucella* sp, human herpes virus 6, retroviruses, and enteroviruses have all been implicated, the role of an infectious agent is at present obscure.

The immune abnormalities in CFIDS reflect abnormalities of baseline regulation. Circulating interleukin-2 levels can be elevated, as can the number of lymphocytes, particularly CD8, bearing activation markers including HLA-DR. Despite apparent increased activation, when challenged, the CFIDS immune system responds inadequately. Delayed hypersensitivity and in vitro mononuclear proliferation are depressed when a patient's lymphocytes are exposed to pokeweed mitogen or phytohemagglutinin. Natural killer cells are also frequently suppressed, a defect only partially corrected by the addition of interleukin-2.

All of this information is preliminary and requires confirmation in studies using appropriate disease controls (ie, patients with depression, fibromyalgia, and atopy). At the same time, the activated state of the immune system provides some evidence that many of the symptoms experienced by CFIDS patients have a physiologic basis.

DIAGNOSIS AND TREATMENT

As already implied, fibromyalgia and depression must be excluded as the primary causes of symptoms. Other conditions which must be considered and would require specific treatment include endocrine disorders such as hypothyroidism, and autoimmune diseases such as Sjögren's syndrome.

Experimental therapies for CFIDS, including intravenous immunoglobulin and immunomodulating agents such as polyribonucleotide (Ampligen), have yet to be demonstrated unequivocally effective. At present, treatment is directed at symptoms. A graduated program of frequent, moderate-intensity exercises may help to relieve fatigue. Sleep disturbance may be treated with tricyclic antidepressant drugs, and myalgias and arthralgias with nonnarcotic anti-inflammatory medications. Most importantly, patients must be helped to understand that, in general, long-term prognosis is good and that their symptoms are not due to a more serious disease.

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ASSESSING NEW TECHNIQUES IN CORONARY ANGIOPLASTY

The number of angioplasties performed in the United States has continued to grow with the introduction of improved catheters and the increasing realization that angioplasty is indeed a viable option for many patients. New techniques are being designed to meet the many treatment challenges. But the recent proliferation of newer technologies has been daunting for many interventional cardiologists. Clinicians need to know the benefits and drawbacks of the new modalities before recommending them or using them in daily practice.

The following brief discussion relates our experience with two of these new techniques over the last 3 years at Boston's Beth Israel Hospital and offers suggestions for integrating these devices into everyday practice.

BALLOON-EXPANDABLE STENTING

Stents serve as internal scaffolds of coronary arteries and provide predictable results and excellent luminal

geometry. The Palmaz-Schatz balloon-expandable stent is constructed of very thin-walled steel tubing with an alternating pattern of slots; it is fitted on a sheathed angioplasty balloon delivery system. When the delivery balloon is inflated within the lesion, each of the rectangular slots becomes a diamond as the stent diameter is enlarged, thereby supporting the inside of the artery. Once the stent is placed, the vessel looks normal. Analysis of more than 250 stents placed at the Beth Israel Hospital showed that the average stenotic diameter of a treated vessel fell from 75% before treatment to −2% after treatment: that is, the stented segment was made slightly larger than the adjacent, untreated segment.

The main drawback to metallic stents has been thrombosis formation. However, a regimen of aspirin, dipyridamole, and oral coumadin appears to keep the thrombosis rate low (approximately 2.9%). Beth Israel Hospital experienced a rate as low as 0.5%. This is much below the 24% early thrombosis rate recently reported with the self-expanding Medinvent stent.

With stents, as with any angioplasty technique, restenosis can occur. After the stent is placed, it is covered with a neointima consisting of proliferative smooth muscle cells. If this neointima remains thin, the lumen continues to look much as it did immediately after stent placement. However, more extensive neointimal hyperplasia (occurring in 15% to 20% of patients) may lead to restenosis within the stent. Fortunately, restenosis within the stent is easily dilated, since the steel mesh confers plasticity to the vessel: the re-dilated artery retains the full lumen size of the inflated balloon. In addition, the neointima is tough and does not crack as easily as atherosclerotic plaque, although the incidence of subsequent restenosis appears to be 30% to 50%.

DIRECTIONAL ATHERECTOMY

The directional atherectomy catheter appears to be particularly useful in treating eccentric or ostial lesions and lesions at the origin of the left anterior descending (LAD) coronary artery. The Simpson AtheroCath consists of a steel cylinder with a window in one side and a low-pressure positioning balloon attached to the other side. As the balloon is inflated, it presses the window against the atherosclerotic plaque, activating a drive unit that turns a cup-shaped cutter, which is advanced slowly across the window. Any plaque that hangs down into the window is shaved away and trapped in the tip of the catheter, leaving behind a large, smooth lumen.

Directional atherectomy appears to provide a predictably larger lumen than conventional angioplasty, with an average 2.2-mm increase in stenotic lumen diameter compared with baseline, and a residual stenosis averaging 5%.

The primary reason for failure of directional atherectomy is the inability to advance the rigid atherectomy housing across calcified lesions or lesions distal to tortuous vessels. However, most such lesions can then be dilated successfully with conventional percutaneous transluminal coronary angioplasty catheters. The procedure's main drawback is its inability to reduce the restenosis rate to below about 30%. Further study is needed.

WHAT IS SUCCESS?

The lack of standardized definitions has made assessment of success, complication, and restenosis rates of these new technologies difficult. The success of conventional angioplasty is easy to define: one must cross the lesion, improve the diameter of stenosis by at least 20%, and leave a residual stenosis less than 50%, without causing a major complication. But for new technologies one needs to know the type of patient the device was used in, the goal of the procedure, and whether the device was used alone or as preparation for subsequent treatment with another device. Restenosis is even harder to evaluate. Multiple baseline factors such as age, sex, vessel size, and prior restenosis must be considered. For new technologies, however, the best definition is perhaps based on an absolute degree of diameter stenosis at the time of follow-up. We prefer the definition of restenosis as stenosis greater than 50% at a follow-up of 6 months, but we have recently introduced the concept of continuous rather than dichotomous definitions of restenosis based on quantitative analysis of the acute and follow-up angiograms.

SUMMARY

New devices for coronary intervention have been used in thousands of patients over the past several years. Although most such devices are still investigational, they hold promise in eliminating some of the hindrances to the broader, more successful use of conventional angioplasty. These new devices seem more effective than conventional angioplasty in treating eccentric or ulcerated lesions, ostial stenosis or stenosis of the LAD artery, disease in older saphenous vein grafts, restenotic lesions after prior intervention, and dissected vessels with actual or threatened abrupt closure. The difficulty facing each clinician is deciding which device to use

under which circumstances in order to provide the safest, most durable, and most cost-effective treatment for the individual patient. Careful and critical analysis of the growing body of information regarding experience with these newer devices will be needed in order to accomplish this goal.

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CONTINUING MEDICAL EDUCATION CALENDAR

APRIL

- **10th Annual surgical pathology symposium**
  April 11
  Symposium director:Ralph J. Tuthill, MD

- **Biostatistics in medicine**
  April 27–28
  Symposium director: Gerald J. Beck, PhD

- **Update in clinical rheumatology**
  April 29–30
  Symposium director: Ali D. Askari MD

MAY

- **Detection of septicemia**
  May 1
  Symposium director: John A. Washington, MD

- **Update on the diagnosis & treatment of headaches**
  May 13
  Symposium director: Robert S. Kunkel, MD and A. David Rothner, MD

- **The restenosis summit IV**
  May 28–29
  Ritz-Carlton Hotel, Cleveland, Ohio
  Symposium director: Eric J. Topol, MD

- **International symposium on advances in pain management**
  May 28–31
  Stouffer Tower City Plaza Hotel, Cleveland, Ohio
  Symposium director: Michael Stanton-Hicks, MD

- **Internal medicine board review**
  May 31– June 5
  Stouffer Tower City Plaza Hotel, Cleveland, Ohio
  Symposium director: David L. Longworth, MD and James Stoller, MD

JULY

- **Medical problems of musicians & dancers**
  July 30–August 2
  Aspen, Colorado
  Symposium director: Richard J. Lederman, MD and Alice G. Brandfonbrener, MD

AUGUST

- **Summer seminars in dermatology**
  August 7–9
  The Ritz-Carlton Hotel, Cleveland, Ohio
  Symposium director: Kenneth J. Tomecki, MD

- **CCF Alumni reunion**
  August 14–15