The heart of the matter

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Selecting a few items for emphasis from the therapeutic wizardry that erupted in cardiology in 1997 is a Hobson's choice. Important developments are evolving in the areas of coronary intervention, antithrombotic therapy, heart failure management and catheter ablation of arrhythmias. Far from comprehensive, this list of topics reflects an informal consensus among a group of academic clinical cardiologists on the most meaningful developments in the past year.

Intracoronary stenting

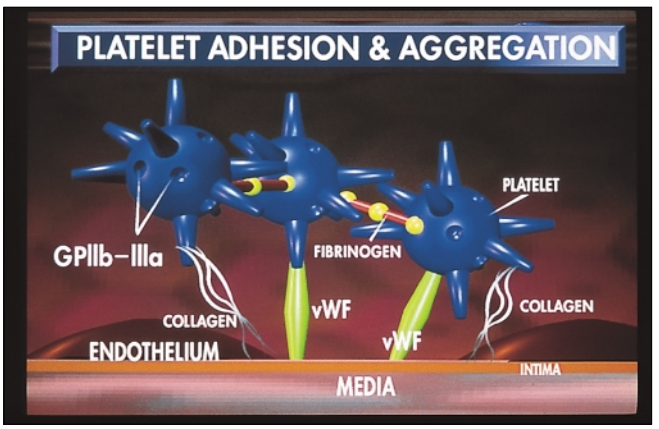
In 1997 interventional cardiologists discovered their version of crack cocaine, the easy-to-use intracoronary stent. We enjoy such a good selection of easily deployed, safe, effective stents, that in many Canadian centres 80% of patients eligible for coronary angioplasty receive these tiny endovascular culverts. No longer used just to finesse suboptimal results, stents afford a larger luminal diameter and reduced recoil, and thus result in fewer early complications and a 25%–40% lower restenosis rate. High-pressure stent deployment and antithrombotic therapy permit routine discharge home the morning after.

Intriguing preliminary clinical reports of the efficacy of intracoronary radiotherapy demonstrated further reduction in the restenosis rate among predisposed patients.[1] In a small study, radiation was administered as iridium-192 gamma-emitting beads; the 6-month restenosis rate was reduced from 54% to 17% without early complications ($p = 0.01$). A number of outstanding issues remain, including the role of stenting versus coronary angioplasty alone, the appropriate dose, timing and type of radiation, proper patient selection, and long-term outcome in terms of vessel patency and freedom from aneurysms.[2] Although stents are a ubiquitous feature of the intracoronary landscape, other adjunctive measures such as IIB/IIIA glycoprotein receptor inhibitors to suppress intracoronary thrombosis are useful. However, the problem of restenosis due to intimal proliferation is extremely complex, involving a number of cell types and growth factors. No suitable animal model exists. Solutions to the restenosis conundrum will evolve slowly, at great expense.

Platelet IIB/IIIA glycoprotein receptor blockade

The antithrombotic efficacy of intravenous IIB/IIIA glycoprotein receptor blockade to inhibit platelet aggregation in acute ischemic syndromes is well established. The platelet surface is populated with 40 000 IIB/IIIA glycoprotein receptors that mediate the final common pathway of platelet activation (see diagram). A number of inhibitors of this receptor have been devised, including modified antibodies and synthetic derivative compounds, with varying degrees of specificity.

Inhibition of thrombus with abciximab, the monoclonal antibody fragment c7E3, in the setting of unstable angina or following conventional coronary angioplasty has significantly reduced the incidence of myocardial infarction and the need for rescue angioplasty for abrupt vessel closure.[3] The 3-year follow-up data from the EPIC Investigation reveals a tendency toward a sustained reduction in combined events, particularly the need for revascularization. This lasting benefit may relate to the cross-reactivity of abciximab with the vitronectin recep-



Essential components of platelet adhesion and aggregation. Integrin adhesion molecules are shown as glycoprotein IIB/IIIA receptors on the platelet surface. They bind specific adhesion ligands such as fibrinogen, von Willebrand factor (vWF) and vitronectin. These elements initiate platelet activation and thrombus development at endothelial sites of vascular injury. Reprinted, with permission, from Eli Lilly Canada Inc.

tor. This integrin is abundant on the surface of smooth muscle and activated endothelial cells, both of which are implicated in restenosis and the development of atherosclerosis.

However, in the cost-conscious Canadian milieu, the impact of these elegant new drugs can be more virtual than real owing to their high price tag. Consequently, most centres have developed guidelines limiting their use to intractable thrombotic catastrophes.

The relative merits of abciximab versus stenting are being addressed in the EPILOG-Stent Trial. Although an evidence-based choice favouring one therapy over another for acute ischemic problems involving thrombus is not yet possible, current Canadian practice suggests that stenting is a more efficient way to achieve a greater luminal diameter and a lower restenosis rate.

Managing heart failure

Congestive heart failure exacts a huge toll from Canadians, causing 4000 deaths annually. Advocated for more than 20 years, β-blocker therapy is now established treatment. β-Blockers inhibit the sympathetic overactivity associated with congestive heart failure that correlates with reduced survival. A meta-analysis of 17 randomized clinical trials of β-blocker therapy for congestive heart failure showed a decrease of 31% in the death rate, with 1 death prevented per 35 patients treated.[4] This reduction was most impressive with carvedilol, a combined α–β-blocker, than with other β-blockers.

The efficacy of carvedilol versus conventional β-blockers is being addressed in a large randomized trial. Although most patients with left heart failure and ventricular dysfunction should be given a β-blocker, it is premature to advocate carvedilol as the exclusive choice. The relative benefits of β-blocker therapy for heart failure are apparently additive to those achieved with angiotensin-converting enzyme (ACE) inhibitors.

Another intriguing development in the treatment of congestive heart failure is the possible efficacy of angiotensin II receptor blockers such as losartan.[5] The ELITE Study involving older patients found that, compared with captopril, losartan was better tolerated and demonstrated a lower all-cause mortality rate among patients with NYHA class II–IV congestive heart failure (4.8% v. 8.7%; risk reduction 46%, $p = 0.035$). Recently, the RESOLVD trial, comparing candesartin and enalapril, was stopped prematurely because of a lack of efficacy. Resolution of this issue must await results of the larger ELITE II trial, currently under way. For patients who cannot tolerate ACE inhibitors, angiotension II blockers may prove to be a good alternative.

Catheter ablation of arrhythmias

The stunning achievements in the electrophysiology lab have emancipated scores of patients from a lifetime of burdensome antiarrhythmic drugs. Highly successful radiofrequency catheter ablation of accessory pathways has revolutionized our approach to re-entrant supraventricular tachycardia.

More recently, experience with the multi-electrode "halo" catheter has led to effective ablation of medically refractory atrial flutter.[6] The isthmus in the low right atrium incorporating the tricuspid annulus is an important part of the re-entrant loop in atrial flutter. Radiofrequency ablation of this site results in a permanent block of electrical activity in both directions, thus interrupting the re-entrant cycle.

Atrial fibrillation remains a challenge to the electrophysiologist. The concept of multiple wandering re-entrant wavelets requires a "critical mass" of atrial tissue for atrial fibrillation to develop. This has led to innovative techniques for surgical and radiofrequency ablation in the search to control atrial fibrillation. However, much remains to be learned about the electrophysiology of atrial fibrillation, and new ablation techniques continue to evolve.

References

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