Cardiovascular Therapies in the 1990s
An Overview

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Summary
Cardiovascular medicine has evolved steadily over the past two decades. Inspired by progressive declines in the overall incidence and mortality rates from cardiovascular diseases, emphasis has been placed on 3 specific areas: prevention, early diagnosis, and aggressive intervention.

During the decade spanning the 1980s, impressive strides were made in many areas – diagnostic and therapeutic alike. However, an observed reduction in patient mortality stemming from acute myocardial infarction was particularly gratifying. Clearly, the large scale use of thrombolytic therapy and postinfarction strategies designed to prevent reinfarction, limit ventricular dilation, and reduce cardiac death figured prominently. Despite these encouraging facts, however, coronary heart disease remains the leading cause of death in Western society, and thrombolytic therapy is still not being utilised by the medical community to its full potential. Furthermore, adjuvant therapy, during both the early and the late phases of acute myocardial infarction, is being instituted inconsistently, and at times haphazardly. Arrhythmia management and the prevention of sudden cardiac death require further investigation, as does the treatment of chronic congestive heart failure, and the prevention of coronary atherosclerosis.

This overview provides a state-of-the-art review and look into the future of 5 critical areas: acute myocardial infarction, adjuvant treatment strategies for acute myocardial infarction, cardiac arrhythmias, chronic congestive heart failure, and hyperlipidaemias.
Cardiovascular medicine, as with other areas of medicine and science, continues to evolve at an astonishing pace. The decade spanning the 1980s was highlighted by striking progress in molecular biology, biochemistry and genetics, and by exciting scientific advances in diagnostic and therapeutic technology including magnetic resonance imaging, radionuclide imaging, echocardiography, coronary angioplasty and fibrinolytic therapy.

The 1990s promise to be equally exciting, with emphasis likely to be placed on further development of pharmacological therapies for acute myocardial infarction, congestive heart failure, hyperlipidaemias and cardiac arrhythmias.

1. Acute Myocardial Infarction

Acute myocardial infarction may be defined as sudden irreversible damage to the myocardium resulting from a critical imbalance between oxygen supply and demand. With rare exceptions, it is caused by an occluding coronary artery thrombus at the site of a ruptured atherosclerotic plaque. Although the treatment of myocardial infarction will undergo further evolution in the 1990s, specific pharmacological agents with proven benefit will continue to play important therapeutic roles.

1.1 β-Adrenergic Blocking Agents

β-Adrenergic blocking agents reduce myocardial oxygen demand through a reduction in heart rate, systemic blood pressure and myocardial contractility (Wolfson & Gorlin 1969). When given intravenously within 12 hours of symptom onset, β-blockers have been shown to reduce both infarct size and the incidence of complex ventricular arrhythmias (Yusuf et al. 1983). To date, many randomised trials have been conducted, involving over 27 000 patients, examining the impact of β-blockers on (early) mortality, reinfarction, and cardiac arrest. Overall, β-blocker therapy has decreased early mortality by 13%, and significantly reduced the incidence of reinfarction and cardiac arrest (Yusuf et al. 1985).

In the recently completed Thrombolysis in Myocardial Infarction phase II (TIMI-II) trial (TIMI Group 1989), a subgroup of 1390 patients with acute myocardial infarction were assigned randomly to immediate intravenous β-blockade (metoprolol), followed by oral metoprolol, or oral metoprolol begun on postinfarct day 6. All patients also received intravenous alteplase (r-TPA). While inhospital and 42-day mortality rates did not differ significantly between groups, patients given immediate β-blocker therapy did experience fewer recurrent ischaemic events and nonfatal reinfarctions. Moreover, patients in a low risk subgroup who were treated with alteplase and intravenous metoprolol within 2 hours of symptom onset appeared to derive the maximum benefit, experiencing a significant reduction in cardiac events (death, recurrent myocardial infarction).

At present, a wide variety of β-adrenergic blockers are either available or in advanced stages of development. β₁-Selective agents, including acebutolol, betaxolol, bevantolol, bisoprolol, celiprolol and esmolol, may offer advantages over other β-adrenergic blockers in acute myocardial infarction, but clinical research is required. β-Adrenergic blockers with α₁-antagonistic properties, such as bucindolol, celiprolol and labetalol, may also yield beneficial effects by reducing myocardial wall stress in the early stages of infarction (Frishman 1981, 1988). With rare exceptions, β-adrenergic blockers with intrinsic sympathomimetic activity (ISA) have not been beneficial (Australian and Swedish Pin dolol Group 1983; European Infarction Study Group 1984; Frishman et al. 1984). Further experience with newer β-adrenergic blockers such as carvedilol, dilevolutol and carteolol will be obtained in the 1990s.

The long term beneficial effects of β-adrenergic blockade following acute myocardial infarction are well known (Goldman et al. 1988).

1.2 Nitrates

Nitrate preparations exert a favourable effect on myocardial oxygen demand by reducing both left ventricular filling pressure (preload) and myocardial wall stress (afterload) [Jugdutt & Warnica 1988].