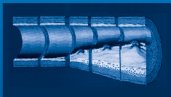


Preventive Cardiology

*Insights Into the Prevention
and Treatment
of Cardiovascular Disease*
SECOND EDITION

Edited by

JoAnne Micale Foody, MD



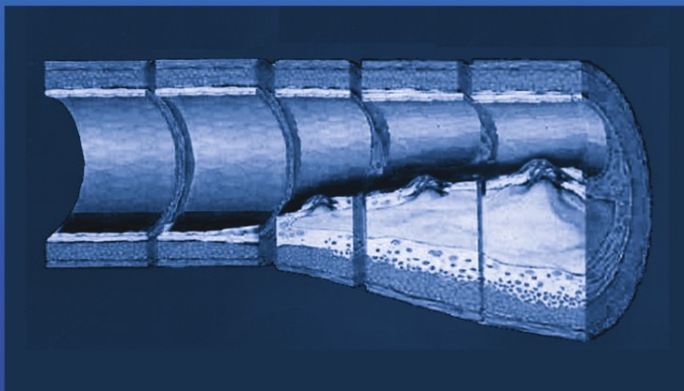
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SECOND EDITION

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PREVENTIVE CARDIOLOGY

*Insights Into the Prevention and Treatment
of Cardiovascular Disease*

Second Edition

Edited by

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PREFACE

Preventive cardiology is a fast moving field that places emphasis on the prevention and treatment of coronary disease. *Preventive Cardiology: Insights Into the Prevention and Treatment of Cardiovascular Disease, Second Edition* is intended for clinical cardiologists, internists, primary care providers, and allied health care professionals who wish to extend their knowledge and expertise in the rapidly expanding field of preventive cardiology. It is the mission of this book to provide clinicians with the understanding and tools necessary to implement prevention in their daily practices.

Recent changes in the delivery of health care in the United States and abroad, in conjunction with new scientific evidence supporting the role of preventive strategies in the maintenance of cardiovascular health, have focused new attention and efforts on the field of cardiovascular disease prevention. The field of cardiology is thus making a gradual transition from the technology-driven, intervention-oriented perspective of the last several decades to a new, preventive, molecular-based perspective. As fresh evidence amasses that preventive measures produce a considerable decrease in the incidence of both primary and secondary cardiac events and mortality, there is growing, widespread acknowledgment that health care providers from all arenas must initiate preventive strategies in the management and care of their patients.

Preventive Cardiology: Insights Into the Prevention and Treatment of Cardiovascular Disease, Second Edition hopes to provide clinicians with both the knowledge and expertise to incorporate preventive strategies into their everyday practices. It will not only provide practical information for the management of patients at risk for cardiovascular disease, but also offer an overview of the new paradigms in the pathophysiology of coronary artery disease (CAD). The first part of the book focuses on the atherosclerotic process, the important central role of the endothelium in the maintenance of cardiovascular health, and the role of inflammation in CAD. This section provides a novel current perspective on important emerging concepts in the pathophysiology of coronary atherosclerosis.

The second part focuses on traditional cardiovascular risk factors and provides insights into gender-specific aspects of CAD risk. These insights offer thorough, concise reviews of the various risk factors with preventive strategies outlined for the clinician. The final part of the book provides an overview of approaches for the identification of patients at risk for CAD events and reviews of stress testing in patients with CAD and the important role of antiplatelets in coronary disease. Finally, given the imperatives of cost-containment and health care resource allocation, a chapter on pharmacoeconomics of preventive strategies is included. The goal of *Preventive Cardiology: Insights Into the Prevention and Treatment of Cardiovascular Disease, Second Edition* is to provide an overview of the exciting opportunities to prevent the progression, and in some instances to regress the process, of coronary atherosclerosis and incorporate these strategies into the daily practice of clinical medicine.

JoAnne Micale Foody, MD

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I

NEW PARADIGMS IN THE PATHOPHYSIOLOGY OF CORONARY ARTERY DISEASE

1

The Unstable Plaque

Implications and Opportunities for Prevention

JoAnne Micale Foody, MD and Steven E. Nissen, MD

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INTRODUCTION

During this past decade, clinical trials have added to our understanding of the pathophysiology and prevention of coronary atherosclerosis. Evidence is accumulating that cholesterol lowering has immediate consequences that may favorably affect the coronary atheroma and subsequent coronary events. Intravascular ultrasound (IVUS) provides a new modality by which to better understand the atheroma.

CORONARY HEART DISEASE: AN OVERVIEW

In the United States, approx 14 million adults have a current diagnosis of coronary heart disease (CHD) ([1](#)). One-third of the 1.5 million individuals who experience myocardial infarctions each year will die. The estimates of the financial costs (i.e., treatment and lost wages) that are associated with CHD in Americans range between \$50 billion and \$100 billion per year ([1,2](#)). Although the incidence of death from CHD has decreased in the United States, the total number of deaths from CHD has recently begun to increase

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after a previous steady decline. Most likely, this is the result of the increased number of middle-aged and elderly people in the population. Clearly, primary and secondary CHD prevention measures that are more effective are required. CHD prevention in the future will be the result of the ground-breaking research that has been conducted during the past 25 yr. For example, in the 1970s, data from the Framingham Epidemiological Study demonstrated that increases in serum cholesterol levels in the general population were associated with an increased risk of death from CHD (3–5). In 1988, the National Cholesterol Education Program (NCEP) identified elevated low-density lipoprotein cholesterol (LDL-C) as a primary risk factor for CHD (6). In the 1993 NCEP Adult Treatment Panel II Report, this conclusion was further strengthened by the addition of aggressive dietary and drug therapy recommendations for patients with known CHD (2). In 1995, Gould and associates reported meta-analysis data on 35 randomized clinical trials that lasted longer than 2 yr and were designed to reduce serum cholesterol levels (7). They concluded that for every 10 percentage points of cholesterol lowering, CHD mortality was reduced by 13% ($p < 0.002$) and total mortality by 10% ($p < 0.03$). According to the most recently reported US National Health and Nutrition Examination Survey III, an estimated 5.5 million Americans with CHD should be treated with lipid-lowering medications under the NCEP guidelines (8). Presently, less than one-third of those CHD patients who require lipid-lowering medications actually receive treatment, and only a small proportion of those who do receive treatment achieve NCEP target levels (1). In controlled clinical trials, hydroxymethylglutaryl (HMG)-coenzyme A (CoA) reductase inhibitors have been shown to lower total and LDL-C levels; decrease CHD-related morbidity and mortality in patients with CHD; and slow progression of, and, in some cases, cause regression of coronary atherosclerosis (1,7,9,10).

During the past decade, new scientific evidence strongly supporting the role of preventive interventions in the maintenance of health has focused much needed attention and efforts on cardiovascular prevention. New trials of lipid lowering have added to our understanding of the pathophysiology and prevention of coronary atherosclerosis (11–19). As this new evidence is amassing, there is widespread acknowledgment that lipid lowering with statins should be a mainstay of treatment for the patient with chronic coronary artery disease (CAD). IVUS is a new imaging study that provides the opportunity to more directly view the atheroma and study its response to risk-factor modification.

PATHOGENESIS OF CAD

Classic theory on the pathogenesis of acute coronary syndromes taught that the atherosclerotic process led to plaque formation and subsequent coronary artery luminal narrowing (Fig. 1). At some point, these lesions developed an overlying platelet-containing thrombus that acutely diminished coronary perfusion and resulted in an acute coronary syndrome. A new paradigm for acute coronary syndromes has emerged. New data suggest that most acute coronary syndromes involve coronary artery segments that do not have high-grade anatomic stenoses documented by recent coronary angiograms (20). Moreover, it seems that less stenotic lesions, characterized by thin fibrous caps, large concentrations of soft lipid accumulations, large numbers of monocytes and macrophages, and depletion of smooth muscle cells, cause the majority of acute events (Fig. 2). These “vulnerable plaques” seem highly prone to rupture, thereby allowing blood to come in contact with highly thrombogenic substances found in the lipid plaque (20–22). Reduction of cholesterol may not only decrease the lipid content of the plaque, but can

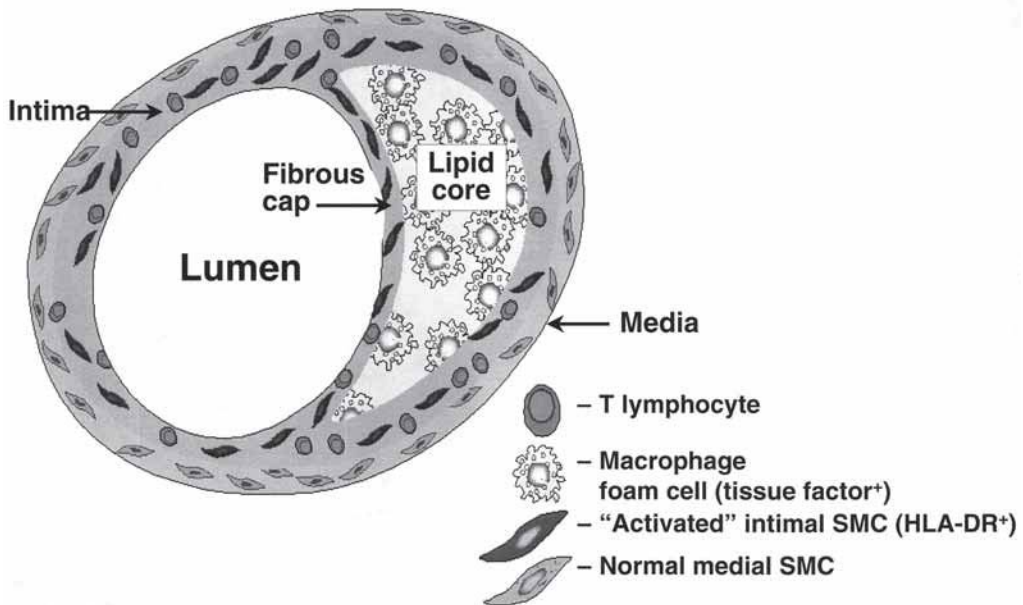


Fig. 1. Unstable plaque. (Adapted from ref. 20.)

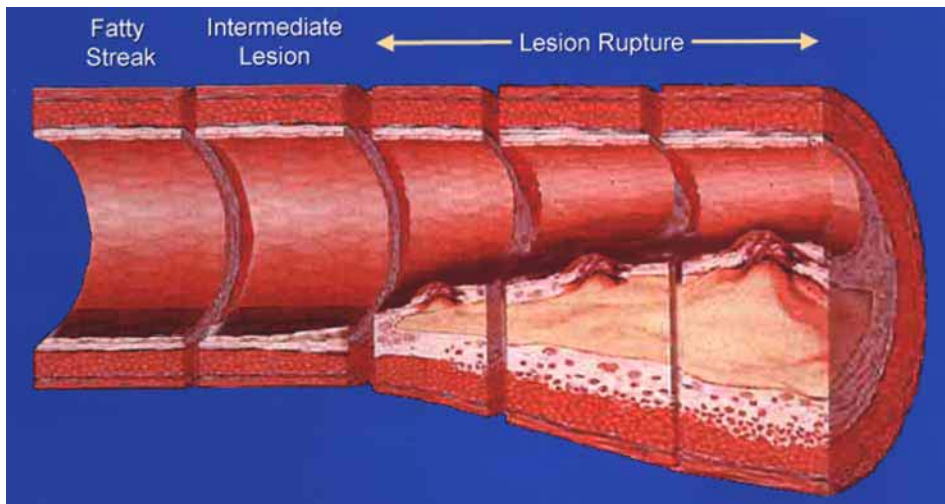


Fig. 2. Conventional wisdom: plaque development.

also reduce the accumulation of monocytes and macrophages, thereby helping to transform these “vulnerable” into less active or “quiescent” plaques ([19,21,22](#)) ([Fig. 3](#)).

This proposed mechanism of plaque stabilization may help to explain why numerous clinical trials using lipid-lowering regimens in patients with CHD have shown that reductions in rates of coronary events and mortality are far greater than would be expected from the results of lesion regression analysis performed using quantitative coronary angiography (QCA) ([4,13,20,23](#)). For example, in the Familial Atherosclerosis Treatment Study,