

# MYOCARDIAL INFARCTION



# MYOCARDIAL INFARCTION

New perspectives in  
diagnosis and management.

Edited by

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# ***Preface***

Despite the great medical advances of the past two decades, there is no evidence that these achievements have affected longevity in the United States. U.S. mortality statistics show an increase in the average life expectancy from 1920 to 1957 of about 13 years for the male and 19 for the female. However, there has been no further improvement since that time, mainly because of mortality from the nation's two biggest killers: cardiovascular disease, which continues to claim some 1,100,000, and cancer, some 330,000 lives in the United States each year.

Half of the cardiovascular deaths are due to myocardial infarction, and of these, almost 250,000 are considered sudden. Fundamentally, improved survival can be achieved for all when methods are developed to prevent or retard the arteriosclerosis process which eventually compromises the circulation to the myocardium and affects performance of the heart as a pump.

The arteriosclerotic process, which starts shortly after birth, appears to accompany aging. At present there is little evidence that any therapeutic measure is capable of reversing this process. Factors have recently been established which increase the risk of arteriosclerosis, such as hypertension, smoking, and abnormal lipid profiles. It is now believed that if these risk factors can be kept at normal levels, the development of premature arteriosclerotic disease process might be retarded.

At long last, congressional authorities seem to recognize the problem of arteriosclerosis and how it affects the health of the nation, strains the health delivery service, creates tremendous expense, and at the same time saps the strength in the form of gross national product. Now some of our congressional leaders have become alarmed and are demanding that scientists increase both the research activities in cardiovascular disease and also the speed of application of new discoveries to the care of the patient. A sharp increase in relevant appropriations is planned in marked contrast to the cutbacks in research caused by limited funding over the 1966 to 1971 period.

When Dr. Robert Grant took over the directorship of the National Institutes of Health in 1965 he appealed to governmental authorities to note that less than 4% of the entire Heart Institute budget was being applied to research the nation's biggest killer, occlusive coronary artery disease. Before he himself died suddenly and prematurely of this scourge, Grant was able to convince Federal authorities to increase the level of funding which could establish special programs for the study of myocardial infarction. It was through his foresight that

nine myocardial research units (MIRUs) were established across the nation to provide new pathophysiologic data on exactly what occurs when a patient sustains a myocardial infarction. It was his belief that only when the physician-scientist understood the multiple and fundamental mechanisms would new and effective forms of treatment follow. It took several years for the MIRUs to be established, and we are just now beginning to feel the impact of new information which undoubtedly will result in new forms for treatment of myocardial infarction. This text, written by the men and women making the discoveries, reveals that we can anticipate new perspectives which offer much hope.

While revising one of our texts, we recognized the unbelievably rapid rate of development for the new techniques in the management of myocardial infarction. The rapidity with which new coronary care unit concepts which were not even conceived a decade ago have been applied to the delivery of health care is amazing. We both participated in the Second Bethesda Conference in 1965 (American College of Cardiology Second Bethesda Conference: Training techniques for the coronary care unit. *Amer. J. Cardiol.* 17:736-747, 1966) to review the individually variable results of some 14 coronary care units established across the country. That conference revealed that the common and essential ingredient to the success of these units could only be attained by the early application of countershock for ventricular fibrillation, by non-physician personnel. Therefore, new training techniques in coronary care had to be established and legal authority obtained for the nurse to apply immediate countershock. This was accomplished rapidly and now coronary care units are a standard facility in some 3,600 hospitals. Since the Bethesda Conference it has been demonstrated that prompt administration of antiarrhythmic drugs such as lidocaine or procaine amide can prevent the occurrence of fatal ventricular fibrillation, when irritability of the heart supervened. Such action has drastically reduced the number of instances of ventricular fibrillation. Some 50,000 lives are now saved in this country each year by these new concepts of early aggressive management of myocardial infarction.

When we assembled the group of experts to provide a course on "New Perspectives in the Diagnosis and Treatment of Myocardial Infarction" for the American College of Cardiology, we structured the program to encompass all aspects of the topic. These authorities who are actually making the discoveries should collectively provide the reader with a text concerned with all aspects between basic science and its application to the delivery of health services. We hope the up-to-date bibliography at the end of each chapter will provide references that will lead the reader into still more comprehensive areas of study.

We are indebted to Mr. William Nelligan, Executive Director of the American College of Cardiology, and his staff for their aid in preparing the program. We are grateful to Dr. Theodore Cooper, Director of the National Heart and Lung Institute, Dr. Peter Frommer, Chief of the Myocardial Infarction Branch of the National Heart and Lung Institute, and Dr. Herbert Gold, who provided abundant support in planning the program. The authors are particularly indebted to Mrs. Jeanne Bloom for her help in preparing the program and the book.

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## ***INTRODUCTION***

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# ***New Research Perspectives in Myocardial Ischemia and Infarction***

**ELIOT CORDAY AND H. J. C. SWAN**

Elimination of heart and blood vessel diseases as significant causes of disability and death could increase the average American life expectancy by about 11 years and provide for annual savings to the economy in lost wages, productivity, and costs of medical care of more than \$30 billion per year.<sup>1</sup> The chief cause of death in the United States, myocardial infarction, accounts for a mortality of over 650,000 per year, and about half of these are sudden and unexpected. Of greater economic and social importance is the significant incidence of cardiovascular deaths in younger persons. The victims, predominantly men, are frequently heads of households unexpectedly taken from their families at the prime of their productive lives.

## **National Priorities**

### *Arteriosclerosis*

Despite extensive research in the prevention of arteriosclerosis and the causative factors of cerebral stroke, myocardial infarction, and other vascular disease, there has been little overall change in their combined mortality of over one million, one hundred thousand lives per year in the United States. The National Heart and Lung Institute's national task force on arteriosclerosis<sup>2</sup> concluded that the totality of existing knowledge, especially as it relates to the basic causes of the disease, does not permit efficient or compre-

hensive control of either atherosclerosis or its complications such as heart disease, stroke, kidney failure, or vascular disease. Thus, the logical recommendations are that this country should 1) without delay develop effective mechanisms for the exploitation of existing knowledge and 2) recognize the necessity of accelerated research programs, seeking information which will afford ultimate control of this important disease. The overriding problem in atherosclerosis is that we do not as yet understand the basic mechanisms underlying the development of the lesions, nor how various risk factors influence the progress of these lesions to the point where signs of clinical disease become evident. Basic investigations into the pathogenesis of the atherosclerotic lesions, including the contribution of hemodynamic forces, the relation of fatty streaks to intimal plaque formation, the role of altered arterial wall metabolism, cellular reaction during lesion formation, transport of lipids across the arterial wall, and the mechanisms of the growth of fibrous plaques, are essential to permit the development of a rational program of prevention and control.

Epidemiologic studies have demonstrated a correlation between clinical manifestations of arteriosclerosis and certain biochemical, physiologic, and environmental factors. These include age, male sex, hypertension, impaired glucose



tolerance, obesity, and hypertension. Other risk factors which may play a role are family history and genetics, gout, physical activity, personality, emotional stress, and mineral content of drinking water. While it is possible on the basis of these risk factors to identify persons especially susceptible to the clinical complications of atherosclerosis, many instances of serious clinical events occur in patients in the absence of these risk factors, indicating that other more important, and as yet unknown, mechanisms must play a dominant role. Although it might take a half century to conduct conclusive clinical trials, some authorities believe a major effort must be made now to develop programs of primary prevention, especially for children and young adults, because such preventative measures may reduce or postpone the onset of complications of atherosclerosis in adult life. Control of these risk factors may also be of value in reducing the incidence of recurring clinical episodes. However, many risk factors are weakly related to the occurrence of clinical events, and their influence on the primary processes of secondary complications is small. Although the strongest association of the risk factors is with hypertension and cigaret smoking, control of these factors in the individual with known coronary artery disease does not reverse the process.

Considering the effects of diet on atherosclerosis, the national Task Force<sup>2</sup> reviewed all the scientific evidence pertaining to the experience with dietary manipulation and incidence of coronary heart disease. The majority of the Task Force members concluded it would be unwise to mount a single major national heart trial in the general population of the United States at this time because such a study might well fail to obtain a definitive scientific answer, and the managerial and logistical problems of accomplishing a well-controlled study are too great. For example, 18% of the total population of the United States relocates annually, so that a period of 7 to 10 years would be

required to obtain a sufficient number of clinical events in the studied population. Accepting even the projected costs of between \$500 million and \$1 billion for such a study, the Task Force concluded that subjects adhering to a given diet regimen would most likely also modify other risk factors, and this might negate some of the basic assumptions of the study and make it difficult to interpret the results.

The benefit of early treatment of mild and moderate hypertension to prevent coronary and cerebral artery disease is now agreed upon.<sup>3, 4</sup> Planned pilot screening programs should now be established utilizing allied health personnel under physician's supervision, for detecting hypertension in adults in selected populations. Once detected they should be referred to their primary physician for treatment. Further basic research into the as yet unknown etiology of essential hypertension, particularly the study of endocrine factors, is vitally required. Additional research must be undertaken to determine the relationship between hypertension, arteriosclerosis, and serious cardiovascular events.

Because of the association of smoking and atherosclerosis and the fact that a high percentage of smokers cannot stop the habit, less dangerous forms of smoking must be substituted. Active support should be established for studies to define the fundamental factors associated with tobacco smoking that contribute directly or indirectly to atherosclerotic disease.

Lack of physical activity is considered one of the risk factors of atherosclerosis and associated serious cardiovascular events. Numerous investigations indicate that those who are more physically active may have less disease and fewer events, but other seemingly high-quality studies do not show this. This statement is also true of certain of the individual relationships between atherosclerosis and smoking, elevated lipid blood pressure, nervous tension, and personality. Possibly, more meaningful relationships could be established if many of these risk factors were

associated together in multifactoral studies.

The Task Force emphasized the great need for further research in atherosclerosis. In his State of the Union Message of January 1972, President Nixon revealed an impatience with the continuing high mortality rate and recommended that the level of federal funding for heart research be increased markedly. Some authorities recommend that accelerated and innovative programs be initiated which would be supervised by a multidisciplinary commission, patterned after the unbelievably successful Missile, Space, and Atomic Energy programs. This new level of funding should stimulate powerful new research programs which could lead to breakthroughs, particularly in prevention and treatment of arteriosclerotic heart disease.

### *Myocardial Infarction*

In the past few years there has been an increasing level of interest in the processes and consequences of myocardial infarction, principally because of encouraging, major programs undertaken by the Myocardial Branch of the National Heart and Lung Institute (NHLI). This agency has implemented studies to reduce death or disability from myocardial infarction. Its diversified program involves fundamental investigations of the electrical, mechanical, and metabolic processes of the myocardium during acute ischemia. It extends to all aspects of ischemic heart disease including the study of clinical manifestations of chronic coronary heart disease and any techniques which might minimize the incidence of sudden cardiac death.

The major portion of the NHLI program has been directed toward the establishment of nine myocardial infarction research units whose tasks are to conduct comprehensive clinical investigation on patients with acute myocardial infarction, to support relevant nonclinical and basic science studies, and to develop some of the requisite tools and methods for clinical research.

The individual programs within the myocardial infarction research units are initiated by the investigators of each unit, but the overall programs must be approved for funding by a national advisory council. The major myocardial infarction research unit objectives include better understanding of ischemic cardiac disease mechanisms and improved detection and diagnosis, as well as prophylactic and acute and chronic therapy. This has necessitated the development of requisite facilities, instrumentation, and computer methods of data collection and reduction.

Investigations have been funded for ways of modifying the acute pathologic processes. New methods have already been developed to measure hemodynamic changes, to assess the amount of infarcted myocardium, and to quantify drug, enzyme, and hormonal influences from blood, which will permit the objective evaluation of therapy. Intensive investigations are also taking place in methods of protecting the ischemic myocardium from progressive and irreversible damage.

### *Sudden Death*

Sudden cardiac death is under study by 19 different contracting organizations across the United States. The objectives of these studies had been carefully outlined by NHLI protocols which called for competitive proposals from national authorities. Those programs considered most promising were funded by contract. Investigations are now in progress to determine physiologic and biochemical processes which are basic to the development of new therapeutic methods for prevention of fatal arrhythmias.

Significant advances have been made recently in the understanding of the alterations of hemodynamic, electrophysiologic, and biochemical function of the heart, as well as with its anatomic correlates during the natural course of myocardial ischemia and infarction. Information about the course of events leading up to sudden cardiac death, the premonitory period of acute myocardial infarction, and