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### Preface
Jagat Narula, Clyde W. Yancy, and James B. Young

### Lessons from Curbing the Coronary Artery Disease Epidemic for Confronting the Impending Epidemic of Heart Failure
William B. Kannel

This article describes five decades of epidemiologic research that has contributed to an explosive expansion of knowledge about the causes and evolution of cardiovascular disease. Cardiovascular epidemiology has become a basic science of preventive cardiology and has provided vital information about predisposing but modifiable risk factors to public health workers, physicians, scientists, and basic researchers. This research also has stimulated national public health initiatives, global attention to cardiovascular disease prevention, and pharmacologic development of agents to control hypertension and dyslipidemia and controlled trials that demonstrate their efficacy.

### The Global Epidemiology of Heart Failure
James B. Young

Heart failure (HF) has become a major clinical and public health challenge. The high prevalence of hypertension and atherosclerotic disease in aging patients relates to this epidemic, as does the ever-increasing problem of obesity and diabetes. Early identification of patients at risk for HF and asymptomatic patients with structural heart disease is critical if the human morbidity and mortality toll and the economic burden that HF causes is to be decreased.

### Risk Factors for Heart Failure
Satish Kenchaiah, Jagat Narula, and Ramachandran S. Vasan

Despite remarkable therapeutic advances in the management of patients with heart failure (HF), the mortality due to this syndrome...
remains high. Identifying free-living individuals who are at high risk for developing HF may allow implementing strategies that can prevent HF. Prospective epidemiologic studies have identified several risk factors and risk markers for HF. This article reviews current knowledge regarding conventional and newer risk markers for HF, outlines possible underlying mechanisms for the increased HF risk, and provides a framework for clinical multivariate risk prediction using HF risk factors.

Genetic Predisposition to Heart Failure
Michele Pasotti, Alessandra Repetto, Luigi Tavazzi, and Eloisa Arbustini

This review describes the numerous and complex molecular systems that are either known players or candidates in heart failure (HF). All systems whose genetic background has been investigated to date in HF are listed and discussed. Discussion also includes functional notes and known genetic polymorphisms already investigated in HF or candidates that have not yet been investigated. Despite substantial research on HF, relatively few coordinated studies have been conducted that assign precise risk to specific genetic polymorphisms. Identification of risk associated with genetic variations and subsequent translation of genetic knowledge into clinical practice will likely progress only in cases of large coordinated studies based on identical standards. The potential result will be a more accurate definition of HF identified as an evolving complex of cardiovascular diseases.

Feasibility of Arresting the Process of Remodeling
P.E. Somasundaram and Y. Chandrashekhar

Heart failure (HF) is a massive public health issue. Ventricular remodeling is pivotal to the pathophysiology/progression of HF and an attractive target for intervention. It currently is believed that interdicting the natural history of ventricular remodeling will be crucial to controlling the HF epidemic. This article reviews the current data on the feasibility of arresting this process. This review is not meant to be exhaustive but provides a brief overview of the approaches being contemplated in this field.

Coronary Artery Disease and Prevention of Heart Failure
Liviu Klein and Mihai Gheorghiade

Coronary artery disease is a major contributor to the progression of left ventricular systolic dysfunction and heart failure (HF). Recognizing that coronary artery disease is a leading cause of HF in the United States is critical to reducing mortality resulting from this condition. Although some patients may be candidates for mechanical revascularization to improve left ventricular function, all patients are candidates for aggressive secondary prevention strategies. This review discusses the prevalence of coronary artery disease, prognostic significance and pathophysiology, risk factor modifications, pharmacologic treatments, and the role of revascularization.
Preventing Heart Failure in Patients with Diabetes
Preethi Srikanthan and Willa Hsueh

Diabetic cardiomyopathy is characterized by a prominent interstitial fibrosis. Postulated etiologies include microangiopathy, autonomic neuropathy, and metabolic factors. A common root of these pathologies is hyperglycemia or hyperinsulinemia, both of which are prominent in type 2 diabetes mellitus, which has the highest incidence of cardiovascular morbidity and mortality. The relative importance of each factor is a matter of debate; it is likely that both of these factors in addition to the concomitant risk factors seen in diabetics (dyslipidemias, hypertension, obesity, coagulation abnormalities) contribute to the spectrum of myocardial disease in diabetes. A discussion of these contributive pathologies and the hyperglycemia and hyperinsulinemia that underlie them is the subject of this review. Treatment methodologies to control the development of such pathology also are discussed.

Mechanisms and Management of Hypertensive Heart Disease:
From Left Ventricular Hypertrophy to Heart Failure
Joseph L. Izzo, Jr, and Alan H. Gradman

Hypertensive heart disease (HHD) is a spectrum of abnormalities that represents the accumulation of a lifetime of functional and structural adaptations to increased blood pressure load. Left ventricular hypertrophy (LVH), increasing vascular and ventricular stiffness, and diastolic dysfunction are prominent intermediate features of this syndrome that operate in parallel with ischemic heart disease and ultimately cause heart failure (HF) if inadequately treated. Outcomes in HHD and HF are improved by antihypertensive drugs at any stage of the condition. This review describes an integrated model of the natural history, pathogenesis, and drug treatment of hypertensive heart disease that is consistent with the recommendations of the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, including an important modification to the HF guideline published by the American College of Cardiology and the American Heart Association that includes LVH and diastolic dysfunction as treatable conditions within the HHD-HF continuum.

Impact of Obesity on the Risk of Heart Failure and Survival After the Onset of Heart Failure
Satish Kenchaiah, J. Michael Gaziano, and Ramachandran S. Vasan

Obesity has reached epidemic proportions in the United States and worldwide. Heart failure (HF) is also a major public health problem, which, despite therapeutic advances, is associated with substantial mortality. The adverse impact of obesity on the cardiovascular system is being increasingly recognized, and includes a hyperdynamic circulation, subclinical cardiac structural and
functional changes, and overt HF. At the same time, the possible protective effect of obesity in patients with established HF has been emphasized in recent studies. This article reviews evidence from epidemiologic studies evaluating the impact of overweight and obesity on the risk of HF, appraises published data on the prognostic significance of overweight and obesity after the onset of HF, describes the potential mechanisms underlying these associations, speculates on the clinical implications of current evidence, and suggests directions for future research.

**Lifestyle and Dietary Modification for Prevention of Heart Failure**

David L. Katz

This article discusses the factors that contribute most to systolic and diastolic heart failure (HF): ischemic heart disease, hypertension, obesity, diabetes, and nephropathy. Diabetes often follows the insulin resistance syndrome in which obesity and hypertension are combined with dyslipidemia, and obesity is likely causal. Diabetes and hypertension are common causes of nephropathy, which in turn is a common precursor to HF. Insulin resistance, obesity, dyslipidemia, diabetes, and hypertension are risk factors for atherosclerotic coronary disease and left ventricular ischemia. Each is also a risk factor for diastolic dysfunction.

**Heart Failure in Women**

Lars H. Lund and Donna Mancini

Women who experience heart failure (HF) exhibit distinct differences from men. Because women are a minority in major HF trials and because diagnostic criteria have been variable in epidemiologic surveys, many questions remain unanswered. This article describes differences in sex hormone effects and responses to injury, pressure overload, and aging, which may account for differences observed in epidemiology, risk factors and causes, mechanisms for disease development, response to treatment, and outcomes. Hypertension, diastolic dysfunction, diabetes, obesity, and inactivity are more important factors in women, whereas ischemic heart disease and systolic dysfunction are more important factors in men. Women appear to benefit less from established treatments but have better survival. Future studies directed exclusively at women may be warranted to confirm or establish benefits of existing and future treatments.

**The Prevention of Heart Failure in Minority Communities and Discrepancies in Health Care Delivery Systems**

Clyde W. Yancy

This article discusses risk factors for cardiovascular disease in the minority community, including hypertension, obesity, diabetes, and diet. The minority community exhibits important population
differences regarding risk and outcomes for cardiovascular disease. The complete explanation for these differential outcomes is lacking and likely to be multifactorial in origin; however, disparities in health care (differences in the quality of health care that are not due to access-related factors or clinical needs, to preferences, or to the appropriateness of the intervention) may emanate from decisions made by the patient, provider, or health care system. Hypertension as a disease entity is strikingly pathologic in African Americans. Correspondingly, the incidence of cardiovascular mortality due to hypertensive heart disease is fourfold higher in African Americans than in non-Hispanic whites. Hypertension and heart failure can be treated effectively in the minority community with a regimen of agents not dissimilar from that used for the general population. Treatment regimens should be individualized based on the disease presentation, associated comorbidity, and disease severity and not on something as arbitrary as race.

Epilogue

Practice Guidelines: Role of Internists and Primary Care Physicians

Shashank Desai and Mariell Jessup

This article discusses practice guidelines for internists and primary care physicians who care for patients at risk for heart failure (HF). These guidelines include identifying the risk factors for the development of HF, identifying patients at risk for the development of HF, learning guideline goals for treatment and other recommendations concerning the management of patients at risk for HF, performing serial assessment of how well guideline goals have been met in patients at risk for HF, performing serial assessment of patients at risk for HF to determine possible progression of disease, considering consultation with other health personnel for patients with progressive stages of HF, enlisting hospitals and other care facilities to promote evidence-based management of patients in all stages of HF, and accessing educational materials for patients and other health care personnel.