Cardiovascular Diabetology:
Clinical, Metabolic and Inflammatory Facets
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Jeffrey S. Borer, New York, N.Y
To my wife Elsa Meryn Fisman, our daughters Gabriela and Dana, our grandchildren Rotem, Guy, Ethan and Einav. To my parents of blessed memory. In gratitude to my beloved family, who in countless ways provides unlimited support, encourages my labor and enriches my existence.

E.Z. Fisman

To my wife, Helena, my best friend and colleague, to our kids, Ilan and Oren who stood by me so strong when I needed them the most. To my mother and father of blessed memory. To a loving family that exceeds my hopes and dreams.

A. Tenenbaum
Contents

IX Contributors

XI Preface
Fisman, E.Z. (Holon); Tenenbaum, A. (Tel-Hashomer)

1 Hyperglycemia and the Pathobiology of Diabetic Complications
Aronson, D. (Haifa)

17 Endothelial Dysfunction in Normal and Abnormal Glucose Metabolism
Esper, R.J.; Vilariño, J.O.; Machado, R.A.; Paragano, A. (Buenos Aires)

44 Biomarkers in Cardiovascular Diabetology: Interleukins and Matrixins
Fisman, E.Z. (Holon); Adler, Y.; Tenenbaum, A. (Tel-Hashomer)

65 Arterial Elasticity in Cardiovascular Disease: Focus on Hypertension, Metabolic Syndrome and Diabetes
Cernes, R.; Zimlichman, R.; Shargorodsky, M. (Holon/Tel-Aviv)

82 Hypertension and Diabetes
Grossman, E. (Tel-Hashomer); Messerli, F.H. (New York, N.Y.)

107 Impaired Glucose Metabolism and Cerebrovascular Diseases
Tanne, D. (Tel-Hashomer/Tel-Aviv)
114 Impact of Metabolic Syndrome in Patients with Acute Coronary Syndrome
   Feinberg, M.S.; Schwartz, R.; Behar, S. (Tel-Hashomer)

127 Optimal Management of Combined Dyslipidemia: What Have We Behind Statins Monotherapy?
   Tenenbaum, A. (Tel-Hashomer); Fisman, E.Z. (Holon);
   Motro, M.; Adler, Y. (Tel-Hashomer)

154 Non-Insulin Antidiabetic Therapy in Cardiac Patients: Current Problems and Future Prospects
   Fisman, E.Z. (Holon); Motro, M.; Tenenbaum, A. (Tel-Hashomer)

171 Subject Index
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The prevalence of obesity, metabolic syndrome and diabetes, which we previously defined as the ‘atherothrombotic chain’, has reached pandemic proportions worldwide. Consequences of diseases related to this atherothrombotic chain such as hypertension, coronary heart disease, peripheral artery disease and stroke account for much of the morbidity in these patients. As a result, our civilization is currently at war against the threatening enemy of cardio-diabetes. The growing understanding of the inter-relationship between diabetes and cardiovascular disease has been reflected by recent guidelines for diabetes and cardiovascular disease to enhance the diagnosis and management of cardio-diabetes. Indeed, effective cardiovascular prevention in patients with obesity, metabolic syndrome and diabetes needs a global strategy, based on knowledge of the importance of different risk factors, both conventional and newly described. In fact, we are currently witnesses and participants of the emergence of a new scientific discipline – Cardiovascular diabetology.

Several independent physiological processes underlie the clustering that defines cardio-diabetes, including insulin resistance, central obesity, dyslipidemia, impaired glucose tolerance, and hypertension. Diabetic arteriopathy, which encompasses endothelial dysfunction, inflammation, hypercoagulability, changes in blood flow, and platelet abnormalities, contributes to the early evolution of these events. Chronic complications of diabetes affecting the cardiovascular system are characterized by a dysfunction of the viscoelastic properties of the arterial vessels and, in particular, of arterial distensibility and compliance. Other nonclassical risk factors such as abnormal oxidized low-density
lipoprotein-cholesterol, adiponectin, interleukins, matrixins and C-reactive protein levels are highly correlated with cardio-diabetes.

Although therapeutic improvements and public health policies for risk factor control have brought about a dramatic reduction in cardiovascular mortality among the general population during the last two decades, this success has not been extended to diabetic patients. The presence of diabetes mellitus increases all-cause mortality and, in particular, cardiovascular mortality by 2- to 4-fold. Furthermore, mortality is dramatically increased in the presence of clinical features such as diabetic nephropathy. Although part of this increase can be explained by interaction with other risk factors and by the clustering of diabetes with other risk elements of the metabolic syndrome, increased cardiovascular mortality and morbidity are essentially conferred by the presence of diabetes per se. Atherosclerotic coronary plaques tend to develop earlier and be more advanced and more diffuse in diabetic patients. Unfortunately, the reperfusion strategies have proven less efficacious in those patients. Percutaneous coronary interventions seem to have a worse outcome in these patients, who are affected by a high incidence of re-occlusion. Due to the frequent coexistence of silent ischemia, this diagnosis is often found too late.

Furthermore, a complex of different adverse characteristics of diabetes, including endothelial dysfunction and a prothrombotic state, augments the probability of plaque instability and occlusion. Diabetes renders patients especially prone to heart failure, resulting from both diffuse coronary heart disease and direct microvascular and myocardial damage. Heart failure is the main cause of death during acute myocardial infarction, the global risk of failure being almost three times higher in the presence of diabetes. The risk of developing significant coronary artery disease is also high in diabetic patients because of the increased frequency of dyslipidemia, which is linked to central obesity and insulin resistance.

The complex and intimate relationship between cardiovascular disease and diabetes is discussed in the following chapters of *Cardiovascular Diabetology: Clinical, Metabolic and Inflammatory Facets* in a ‘crescendo style’ – from basic science to clinical and therapeutic concerns. Beginning with molecular, biochemical, inflammatory and cellular aspects, the book continues with histological and pathophysiologic issues, details particular problems in specific metabolic and clinical settings, and finally analyzes several aspects of clinical pharmacology. The book is made up of nine chapters. In the first, Aronson delineates the biochemical mechanisms by which hyperglycemia induces a large number of alterations in vascular tissue that potentially promote accelerated atherosclerosis. Next, Esper and coworkers clarify how the endothelium is the favorite common target of diabetes and other risk factors, showing that its functional impairment in response to injury occurs long before the development of
visible atherosclerosis. Subsequently, Fisman’s group describes the main features of interleukins and matrixins, features that suggest a common inflammatory basis for both diabetes and coronary disease. Cernes and coworkers discuss the factors influencing the viscoelastic properties of the arterial wall, Grossman and Messerli analyze the several epidemiological and clinical aspects linking diabetes and hypertension, Tanne analyzes impaired glucose metabolism as a predictor of cerebrovascular disease, and Feinberg’s group discuss the impact of metabolic syndrome in patients with acute coronary syndrome. The last two chapters are dedicated to therapeutic issues. Tenenbaum and coworkers talk about the optimal management of combined dyslipidemia, detailing both the classical and modern therapeutic options, and Fisman and coworkers describe the current problems and future prospects of non-insulin antidiabetic therapy in cardiac diabetic patients.

We would like to pay tribute and express our appreciation to the distinguished and internationally renowned co-authors of this book for their outstanding contribution. Despite their many commitments and busy time schedules, these colleagues in Israel, Argentina and the United States enthusiastically stated their acquiescence to cooperate. This book could not have become a reality were it not for their dedicated efforts.

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