Cardiovascular Diabetology:
Clinical, Metabolic and Inflammatory Facets
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Cardiovascular Diabetology: Clinical, Metabolic and Inflammatory Facets

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23 figures and 5 tables, 2008
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
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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 pro-
tein levels are highly correlated with cardio-diabetes.

Although therapeutic improvements and public health policies for risk fac-
tor 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 fea-
tures 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 espe-
cially 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 develop-
oping 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, bio-
chemical, inflammatory and cellular aspects, the book continues with histolog-
ical 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 acceler-
ated 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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