

.....

Preface

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.

Enrique Z. Fisman
Alexander Tenenbaum

.....

Contributors

Yehuda Adler, MD, MHA p. 44, 127

Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel. General Secretary, Working Group on Cardiac Rehabilitation, Israel Heart Society; Medical Director, Shfela Region, Leumit Health Fund; Physician-in-charge, field of Cardiac Rehabilitation and Assistant to the Director General, Sheba Medical Center, Tel-Hashomer, Israel.

Doron Aronson, MD p. 1

Director, Cardiac Care Unit, Division of Cardiology, Rambam Medical Center, Bat Galim, Haifa, Israel.

Solomon Behar, MD p. 114

Medical Director, Israel Society for Prevention of Heart Attack (ISPHA), Neufeld Cardiac Research Institute, Sheba Medical Center, Tel-Hashomer, Israel; Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

Relu Cernes, MD p. 65

Department of Nephrology, Wolfson Medical Center, Holon, Israel; Brunner Institute for Cardiovascular Research, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

Ricardo J. Esper,

MD, PhD, FACC, FAHA p. 17

Professor of Medicine and Cardiology, Universities of Buenos Aires & del Salvador, Buenos Aires, Argentina; Cardiology Consultant, Hospital Militar Central, Buenos Aires; Past-President, Argentine Society of Cardiology, Argentine Foundation of Cardiology, Interamerican Heart Foundation; InterAmerica Representative, Executive Board, World Heart Federation.

Micha S. Feinberg, MD p. 114

Director of Noninvasive Cardiology Unit, Heart Institute, Sheba Medical Center, Tel-Hashomer, Israel; Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

Enrique Z. Fisman, MD p. 44, 127, 154

Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel; Honorary Professor of Cardiology, University del Salvador, Buenos Aires, Argentina; Editor-In-Chief, Cardiovascular Diabetology, BioMed Central, London, United Kingdom.

Ehud Grossman, MD..... p. 82

Professor of Medicine, Vice Dean for Academic Promotions, Sackler Faculty of Medicine, Tel-Aviv University, Israel; Head of Internal Medicine D and Hypertension Unit, Sheba Medical Center, Tel-Hashomer, Israel.

Rogelio A. Machado, MD..... p. 17

Professor of Cardiology and Biostatistics, University del Salvador, Buenos Aires, Argentina; Staff member, Cardiology Service, Hospital Militar Central, Buenos Aires; Chief, Echocardiography Laboratory, Hospital Fancés, Buenos Aires; Member of the Argentine Society of Cardiology.

Franz H. Messerli,

MD, FACC, FACP p. 82

Professor of Medicine, Director, Hypertension Program, Division of Cardiology, St.Luke's-Roosevelt Hospital, Columbia University, New York, N.Y., USA

Michael Motro, MD, FACC p. 127, 154

Full Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

Antonio Paragano, MD..... p. 17

Staff member, Cardiology Service, Hospital Militar Central, Buenos Aires, Argentina; Professor of Cardiology, University del Salvador, Buenos Aires, Argentina.

Roseline Schwartz, MS..... p. 114

Israel Society for Prevention of Heart Attack (ISPHA), Neufeld Cardiac Research Institute, Sheba Medical Center, Tel-Hashomer, Israel.

Marina Shargorodsky, MD..... p. 65

Department of Endocrinology and Diabetes, Wolfson Medical Center, Holon, Israel; Brunner Institute for Cardiovascular Research, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

David Tanne, MD p. 107

Director, Stroke Center, Department of Neurology and Sagol Neuroscience Center, Sheba Medical Center, Tel-Hashomer, Israel; Professor of Neurology, Sackler Faculty of Medicine, Tel-Aviv University, Israel.

Alexander Tenenbaum,

MD, PhD p. 44, 127, 154

Director of Research, Cardiac Rehabilitation Institute, Sheba Medical Center, Tel-Hashomer, Israel. Professor of Cardiology, Sackler Faculty of Medicine, Tel-Aviv University, Israel; Editor-In-Chief, Cardiovascular Diabetology, BioMed Central, London, United Kingdom.

Jorge O. Vilariño,

MD, FACC, FAHA..... p. 17

Chief, Cardiology Service, Hospital R. Gutiérrez, Venado Tuerto, Argentina; Professor of Cardiology, University del Salvador, Buenos Aires, Argentina.

Reuven Zimlichman, MD..... p. 65

Chief of Medicine, Wolfson Medical Center, Holon, Israel; Brunner Institute for Cardiovascular Research, Sackler Faculty of Medicine, Tel-Aviv University, Israel; Professor of Medicine, Sackler Faculty of Medicine, Tel-Aviv University, Israel.