Preface

In the United States, 40 to 45% of those over 60 years of age have the *metabolic syndrome* (1,2,3), and this percentage, based on estimates of the increasing prevalence of excess body weight and the more comprehensive diagnostic criteria for the syndrome, is likely to exceed 60% in newer survey analyses. Children and adolescents, too, are being affected by the metabolic syndrome, in parallel with the increasing prevalence of overweight in young people, now estimated to include 16% of those age 6 to 19 years. Clinicians see with increasing frequency that routine office visits demonstrate the metabolic syndrome, a constellation of discrete but closely related metabolic disturbances indicative of increased risk for (or presence of) cardiovascular disease and/or diabetes. All estimates suggest the increasing impact of the metabolic syndrome on mortality and morbidity (4).

Our aim in developing this new synthesis and analysis of the metabolic syndrome has been to bring together the viewpoints of the epidemiologists, the physiologists, the molecular biologists/biochemists, and the clinicians toward understanding the current state of knowledge of both the causes and the consequences of the metabolic syndrome. These writers aim to stimulate new thinking concerning underlying mechanisms and to encourage heightened efforts to develop new therapeutics, potentially targeting uniquely intersecting pathways or points of intervention. This book is an extended call to action to slow or halt the rising tide of the metabolic syndrome (5).

The metabolic syndrome, including the links among its features, its underlying causes, and its recognized clinical importance, provides the framework for this book, which considers the current status of both basic and clinical science. This is part of a series initiated by G. Reaven and A. Laws (eds.), with *Insulin Resistance: The Metabolic Syndrome X* (Humana Press, 1999). By design, it builds upon two other prior volumes: E. Shafrir and B.C. Hansen (eds.), *Insulin Resistance and Insulin Resistance Syndrome* (United Kingdom: Harwood Academic Publishing, 2002), and B.C. Hansen, J.A. Saye, and L.P. Wennogle (eds.), *The Metabolic Syndrome X: Convergence of Insulin Resistance, Glucose Intolerance, Hypertension, Obesity and Dyslipidemias—Searching for the Underlying Defects* (*Annals of New York Academy of Sciences*, New York, NY, 1999). During these eight years, many of the concepts of the metabolic syndrome have been examined, tested, and strengthened, and, while the basic parameters remain, our thinking about this syndrome and its treatment has undergone considerable refinement.

Major progress has been made in understanding the importance of this syndrome, and in recognizing it as a clinical diagnosis through its inclusion, in 2001, as a new (ICD-9-CM) code (277.7) termed the *dysmetabolic syndrome*.

The interrelationships between metabolic syndrome features and the utility of a metabolic syndrome diagnosis are debated by several authors, with the current but limited conclusion concerning treatment that the best approach may be to treat ". . . individually and aggressively all cardiovascular disease risk factors, . . ." and to treat all collectively as therapeutic agents and new developments allow. Acceptance of risk factor clustering

(obesity, hyperglycemia, elevated triglycerides and low HDL cholesterol levels, hypertension) is shared by all authors, although their perspectives vary widely on the interpretation of this undisputed fact. Both obesity and insulin resistance are frequently named as underlying or predisposing features of the metabolic syndrome; however, multiple metabolic disturbances have now been identified as early markers and potential contributors to the underlying pathology, including inflammatory cytokines and adipokines, endothelial dysfunction, tissue-specific defects in insulin action and signaling, oxidative stress, ectopic lipid deposition, and disordered neuroregulation.

Beyond the basic features of the metabolic syndrome lies a sophisticated array of pathway alterations, for example, in the complex profiling of the dyslipidemia, together with its multi-organ sources of disturbances.

While the first line of treatment, sometimes referred to as *lifestyle modifications*, including diet to produce weight reduction and reduce adiposity and exercise as a general health modifier, remains, more aggressive attention to medically modifying the specific features of the metabolic syndrome toward healthier levels is broadly supported by the authors.

Metabolic syndrome today is one of our most challenging health problems and one with an extraordinary need for early intervention and prevention to slow or halt its progression. Only through an understanding of the science underlying this syndrome can successful interventions be developed and implemented. The editors welcome your input and dialog as together we advance the field of metabolic syndrome and its prevention/treatment.

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