

英文影印版

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# 埃伦堡—里弗金斯糖尿病学

## ELLENBERG & RIFKIN'S DIABETES MELLITUS

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第 5 版

fifth edition

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*Daniel Porte, Jr. • Robert S. Sherwin*



科学出版社

McGraw-Hill

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# PREFACE

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This fifth edition of *Ellenberg and Rifkin's Diabetes Mellitus: Theory and Practice* incorporates many changes.

Molecular and cellular biology have continued to enhance our basic understanding of metabolism, leading us to introduce major revisions in the material covered in the basic chapters. New chapters have been added on the use of molecular techniques in diabetes research and on the cellular biology of the endocrine pancreas. Insulin action is detailed at the molecular level, and much of this new understanding has been put into physiologic and clinical perspective in the chapter on insulin resistance in man. New findings of potentially great significance have led to a new chapter on food intake and energy balance, and new findings of the biochemical basis for macrovascular, microvascular, and neuropathic complications are incorporated into expanded or new chapters. Acknowledging the importance of animal models to understanding the etiology and pathophysiology of diabetes, there is a major revision and update of diabetes in animals in which potential relationships to human diabetes are fully discussed. Additionally, the book begins with a new chapter offering a concise, integrated presentation of body fuel metabolism in health and disease.

The improved understanding of Type I diabetes, or IDDM, and Type II diabetes, or NIDDM, is emphasized by major updates on the pathophysiology of these forms of the disease including a new chapter on basic immunology important to understanding Type I diabetes. Diabetes diagnosis and treatment sections have been expanded to include chapters on mechanisms and management of brittle diabetes; a description of hypoglycemia-induced autonomic failure; hyperlipidemia in diabetes; and the mother in pregnancies complicated by diabetes, including gestational diabetes. New chapters also include a discussion of hypertension in diabetes and the use of insulin and intensified treatment regimens in both Type I and Type II diabetes. The chap-

ter on the relationship of metabolic control of diabetes to the development and progression of long-term complications has been completely revised to include a discussion of all of the major large scale trials including the NIH-sponsored DCCT. Nutritional management has been updated in a chapter which covers both behavioral and traditional nutritional approaches including the most recent recommendations of the American Diabetes Association. An expanded chapter updates the metabolic implications of exercise and physical fitness in the management of diabetes. Two chapters review the current status of whole and segmental pancreas transplantation and various approaches to islet cell transplantation. Each of the chapters in the book provides an up-to-date review by an international authority.

Progress in the field continues at a rapid pace. For example, the first new oral agents have been added to our therapy of Type II diabetes in more than thirty years. Our goal is that information contained in this edition will significantly contribute to improved understanding and treatment of this protean disease.

As is true in all large endeavors, change has occurred in the composition of the authors and the editors. During the preparation of this edition, we were saddened by the illness of our founding editor Harold Rifkin. Harold has been and continues to be the inspirational leader of the editorial team. Fortunately, before his illness, Harold was actively involved in the selection of a new editor, as well as our new authors and chapters. Robert Sherwin, a former student of both Harold Rifkin and Max Ellenberg, had been added to maintain broad editorial perspective and to continue their scholarly tradition. We thank our chapter authors for their dedication to education and scholarly pursuits. We also wish to acknowledge our gratitude to the staff of our new publisher, Appleton & Lange, for their help and support in bringing this book to fruition.

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# INTEGRATED FUEL METABOLISM

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Gerald I. Shulman / Eugene J. Barrett / Robert S. Sherwin

Regulation of fuel metabolism in humans involves a complex interplay between hormones, exogenous nutrients, and interorgan exchanges of substrates designed to maintain a constant and adequate supply of fuel for all organs of the body. The key regulatory hormone orchestrating the exchange and distribution of substrate between tissues under fed and fasting conditions is insulin. Glucagon, catecholamines, cortisol, and growth hormone play major roles in energy regulation during times of acute glucose needs, which occur during exercise, stress, or in response to hypoglycemia (see Chapters 8, 31, and 35). The major organs involved in maintaining fuel homeostasis are the liver and kidney, by virtue of their unique ability to produce glucose; the brain, due to its almost total dependence on glucose as an energy source; and the muscle and adipose tissue, due to their ability to respond to insulin and store energy in the form of glycogen and fat, respectively.

The purpose of this introductory chapter is to review how humans use energy and the means by which the body manages its energy stores during times of feeding, fasting, and exercise. In addition, a brief overview of the impact of diabetes on these processes is presented.

## ■ FORMS OF ENERGY

Ultimately all animals sustain life from the energy released by the breaking of carbon-carbon bonds

formed in plants during photosynthesis. Cellulose is the principal form of this stored energy in the biosphere. It consists of polymers of glucose joined by  $\beta$ 1,4 linkages. In contrast to the  $\alpha$ 1,4 linkages that occur between glucose molecules in glycogen and other edible starches, cellulose is not digestible by humans. However, most ruminants harbor cellulase-producing bacteria in their digestive tracts, which can degrade cellulose to glucose and therefore take advantage of this abundant energy supply.

Energy in foodstuffs exists in three forms: (1) carbohydrate, (2) protein, and (3) fat, which in turn consist of three basic units: sugars, amino acids, and free fatty acids. Glycogen is the main storage form for carbohydrate in humans. It is a macromolecule ( $10^6$  to  $10^8$  kd) consisting of branching chains of glucose bonded by  $\alpha$ 1,4 or  $\alpha$ 1,6 linkages. It is stored by most cells, with the highest concentrations occurring in liver and muscle. Glycogen is highly hydrophilic, with 1 to 2 grams of water stored with each gram of glycogen. Storage of energy in the form of glycogen is therefore relatively inefficient on a weight basis, yielding not the theoretical 4 calories per gram of dry carbohydrate but rather only 1 to 2 calories for each gram of hydrated glycogen.

Unlike carbohydrate, protein is not accumulated in humans as a primary energy reserve. Instead each molecule of protein serves other important biological functions. In the healthy adult human eating a weight-maintaining diet, amino acids derived from ingested protein replenish those proteins that have