

Table of Contents

	Contributors	
	Preface	
1	The Two Phases of Glucose-Stimulated Insulin Secretion: Mechanisms and Controls	3
2	Insulin Gene Regulation	15
3	Processing of the Insulin Molecule	27
4	Electrophysiology of the Pancreatic [beta]-Cell	51
5	Sulfonylurea Receptors, Andenosine Triphosphate-Sensitive Potassium Channels, and Insulin Secretion	69
6	Insulinotropic Glucagon-Like Peptides	99
7	Detrimental Effects of Chronic Hyperglycemia on the Pancreatic [beta]-Cell	115
8	Glucose Toxicity of the [beta]-Cell: Cellular and Molecular Mechanisms	129
9	Lipotoxicity	141
10	Islet Amyloid in Type 2 Diabetes	151
11	Physiologic Action of Insulin	165
12	Integration of Biochemical and Physiologic Effects of Insulin on the Control of Blood Glucose Concentrations	183
13	Glucose Counterregulatory Hormones: Physiology, Pathophysiology, and Relevance to Clinical Hypoglycemia	199
14	The Role of Insulin Receptor Substrate Proteins in Insulin Signaling and Metabolic Regulation	207
15	The Insulin Signaling Network and Insulin Action	225
16	Knockout Mice as a Tool to the Understanding of Diabetes Mellitus	245
17	Regulation of Insulin Action by Protein-Tyrosine Phosphatases	255
18	Small GTPases and Serine/Threonine Protein Kinase Cascades in Insulin Signal Transduction	269
19	Protein Kinase C	301
20	Regulation of Glycogen Synthesis	317
21	Insulin Action on Glucose Transport	335
22	Cellular and Molecular Processes Regulating Glucose Transporter 4 Translocation	349
23	Hormone-Sensitive Lipase, Perilipins, and the Control of Lipolysis in Adipocytes	365
24	Role for Phosphodiesterase 3B in Regulation of Lipolysis and Insulin Secretion	
25	Gene Regulation	383
26	Insulin Degradation	413
27	Insulin and the Ras-Dependent Signaling Pathway	421
28	Germline Manipulation of Glucose Transport and	431

	Glucose Homeostasis	
29	Molecular Links between Peroxisome Proliferator-Activated Receptor-[gamma] and Metabolic Disease	441
30	Definition and Classification of Diabetes Mellitus and the Criteria for Diagnosis	457
31	The Natural History of Autoimmunity in Type 1A Diabetes Mellitus	471
32	Genetics of Type 1 Diabetes	483
33	Autoantibodies and the Disease Process of Type 1 Diabetes Mellitus	499
34	Roles of Cell-Mediated Immunity and Cytokines in the Pathogenesis of Type 1 Diabetes Mellitus	519
35	Major Histocompatibility Locus and Other Genes That Determine the Risk for Development of Type 1 Diabetes Mellitus	539
36	Associations between Immune-Mediated (Type 1) Diabetes and Other Autoimmune Diseases	557
37	Role of Viruses in the Pathogenesis of Type 1 Diabetes Mellitus	575
38	Animal Models of Autoimmune Diabetes Mellitus	591
39	Insights from Transgenic and Gene Targeting Strategies in Type 1 Diabetes	611
40	Diabetic Ketoacidosis and the Hyperglycemic Hyperosmolar Syndrome	627
41	Application of the Diabetes Control and Complication Trial	645
42	Diet Therapy in Type 1 Diabetes Mellitus	659
43	Exercise for the Patient with Type 1 Diabetes Mellitus	671
44	Insulin Therapy and Home Monitoring for Type 1 Diabetes Mellitus	683
45	Immune Intervention	701
46	Islet Cell Transplantation	711
47	Islet Transplantation	721
48	Pancreas Transplantation	733
49	Gene Therapy for Metabolic Disease	747
50	Surrogate [beta]-cells for Insulin Replacement Therapy	763
51	Stem Cells	773
52	Epidemiology of Type 2 Diabetes Mellitus	785
53	Metabolic Abnormalities in the Development of Type 2 Diabetes Mellitus	797
54	Noninvasive Imaging of Insulin Action and Resistance in Humans	809
55	Genetics of Human Obesity	827
56	Obesity: Treatment	839
57	Obesity in Type 2 Diabetes Mellitus	857

58	Effects of Aging Glucose Homeostasis	869
59	Drug-Induced Diabetes Mellitus	879
60	Insulin Secretion in Type 2 Diabetes Mellitus	887
61	Insulin Resistance and Its Consequences: Type 2 Diabetes Mellitus and the Insulin Resistance Syndrome	899
62	Glucose Transporters and Pathophysiologic States	917
63	Glucose Toxicity: Effect of Chronic Hyperglycemia on Insulin Action	939
64	Inflammation, Tumor Necrosis Factor-[alpha], and Insulin Resistance	953
65	Adipokines: Regulators of Metabolic Integration and Energy Metabolism	963
66	Fatty Acids and Insulin Resistance	979
67	Triglyceride in Muscle	987
68	Candidate Genes for Type 2 Diabetes Mellitus	1003
69	Genetic Syndromes Associated with Severe Insulin Resistance: Mutations in the Insulin Receptor Gene and Lipotrophic Diabetes	1013
70	Maturity-Onset Diabetes of the Young: A Model for Genetic Studies of Diabetes Mellitus	1029
71	Rodent Genetic Models of Obesity and Type 2 Diabetes Mellitus	1041
72	Primate Animal Models of Type 2 Diabetes	1059
73	Preventing Type 2 Diabetes: The Diabetes Prevention Program	1077
74	Dietary Therapy in Type 2 Diabetes Mellitus: Spreading the Nutrient Load	1085
75	Exercise in Patients with Type 2 Diabetes Mellitus	1099
76	Insulin Secretagogues: Sulfonylureas, Meglitinides, and Phenylalanine Derivatives	1107
77	Metformin	1123
78	Peroxisome Proliferator-Activated Receptor Modulators	1139
79	[alpha]-Glucosidase Inhibitors in the Treatment of Diabetes	1151
80	Glinides	1163
81	Combination Therapy in Type 2 Diabetes Mellitus	1177
82	Intensive Insulin Therapy for Patients with Type 2 Diabetes	1191
83	Hypoglycemia in Type 2 Diabetes Mellitus	1213
84	New Therapies to Promote Insulin Action	1225
85	Intermediary Metabolism during Pregnancy: Implications for Diabetes Mellitus	1237
86	Effects of Maternal Diabetes Mellitus on Intrauterine Development	1251
87	Pregnancy and Complications of Diabetes Mellitus:	1265

	Maternal and Fetal Implications	
88	Gestational Diabetes Mellitus	1291
89	Pathophysiology of Diabetic Retinopathy	1303
90	Pathogenesis of Diabetic Nephropathy	1315
91	Diabetic Neuropathies: An Overview of Clinical Aspects, Pathogenesis, and Treatment	1331
92	Diabetes Mellitus, Lipids, and Atherosclerosis	1365
93	Pathophysiology of Hypertension in Diabetes Mellitus	1377
94	Macrovascular Complications of Diabetes Mellitus	1401
95	Skin and Diabetes	1411
96	Neonatal Diabetes Mellitus	1423
97	Hypoglycemia in the Adult	1427
98	Biochemistry and Molecular Cell Biology of Diabetic Complications: A Unifying Mechanism	1441
99	Hyperinsulinemia and Insulin Resistance	1457
100	The Role of Growth Factors in the Pathogenesis of Diabetic Microvascular Complications	1469
101	Oxidative Stress, Inflammation, and Diabetic Complications	1485
102	Diabetic Vasculopathy	1503
	Index	1513